The Metabolic Response *to* Neonatal Surgery

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To Isabella Forshall

Preface

The problems associated with the pre- and post-operative management of newborn infants have interested me for a number of years This interest was further stimulated by a visit to the United States, which I undertook five years ago with the aid of a special fellowship from the Commonwealth Fund in New York. My studies convinced me that the pre- and post-operative treatment of neonates was mainly based on clinical experience I therefore attempted to put our treatment on a scien tific basis by investigating the metabolic changes brought about by operation.

This research was carried out on newborn infants admitted under the care of Miss I Forshall and myself to the Neonatal Surgical Unit of Alder Hey Children's Hospital, Liverpool, under the auspices of the Department of Child Health. Financial aid was provided by a grant from the Research Committee of the United Liverpool Hospitals

I should like to thank all my colleagues, who gave me so much of their time in helping and advising me during the progress of this report.

Professor N B Capon, Director of the Department of Child Health of the University of Liverpool, has given me most valuable encouragement during the course of the investigations

Dr. E G Hall, Pathologist to Alder Hey Children s Hospital, has been closely connected with this study from its inception to its completion. He helped to draw up the original plan of research, was largely responsible for supervising the technical side of the investigation, and has been of the greatest assistance in preparing this manuscript. He specifically concerned himself with the investigation of the body fluids, and is responsible for that part of Chapter II describing our methods Without his knowledge and enthusiasm this work would never have been completed.

It would be impossible to carry out such an investigation without the help of a biochemist. We have indeed been fortunate in enlisting the collaboration of Mr J T Ireland, Senior Biochemist to Alder Hey Children s Hospital. Mr Ireland s ingenuity in modifying existing ultra micro tests for blood analysis and in devising new ones

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CHAPTER I

Introduction and Historical Notes

Neonatal surgery, one of the newest branches of general surgery, has made great advances during the last twenty years — mainly under the impetus of the studies conducted in Boston by Professors Ladd and Gross (1941) The fact that the operative mortality — once forbiddingly high — has gradually fallen cannot be ascribed to improvements in the actual surgical technique, as there have been few technical advances during the last ten years. It should be credited, rather, to more efficient pre- and post-operative management. Until recently pre- and post-operative treat ment of neonates has been largely empirical. Since the normal physiology of newborn in fants is as yet little understood and there is considerable disagreement among the author ities about even such a fundamental problem as the function of the kidney during the newborn period, it is not surprising that few data are available on the neonatal response to surgery

The large amount of research carried out during the last few decades on metabolic reactions of older children and adults sometimes obscures the fact that much of the fun damental experimentation was accomplished during the nineteenth century even though the methods of pathological and biochemical investigation available at that time were comparatively crude. In 1839 the Alsatian chem ist J -B Boussingault had carried out the first scientifically accurate metabolic study The "patient" thus analysed for the benefit of future generations was a lactating cow and, significantly, the results of the investigation were recorded, not in a medical or veterinary publication, but in a surgical journal. Meanwhile, Justus von Liebig's studies in organic chemistry had led him to recognize the process of metabolism which he defined as "the sum of chemical changes of materials under the influence of living cells" (Liebig, 1842) This definition has never been improved upon

Throughout the nineteenth century the obvious metabolic responses produced by cholera stimulated scientific interest in the precise nature of the changes. As early as 1831, W B O'Shaughnessy, a British medical practitioner reported the fundamental observation that cholera deprives the body of water and chlorides and suggested that recovery from the disease was facilitated by the restoration of water and salt. O'Shaugh nessy's observations led another British doctor, Thomas Latta, to effect an encouraging improvement in an elderly cholera patient by administering the saline solution intra venously, rather than orally In 1850 a Ger

dangerous than those that occur in the later age groups. This view is supported by the fact that, if certain precautions are taken, these infants stand extensive operations extraordinarily well.

By undertaking this research we hoped to evolve a pre- and post-operative régime based on laboratory as well as clinical evidence, and also to throw some light on the way in which neonates differ from adults in their metabolic response to surgery. To facilitate comparison, we consciously modelled our studies and the presentation of our results on the report on the metabolic response of adults to surgery published in 1952 by Moore and Ball.

At the outset of our study we were handicapped by the lack of precedents. At first we encountered many technical difficulties and these were only gradually overcome. The procedures that we finally found most satisfactory for our purposes are described in Chapter II. Because these ultra micro methods are time-consuming and the supervision of the infants during the studies must be meticulous, we were able to observe only nine cases over a period of nearly three years. The study of these nine cases entailed over 8,500 chemical analyses, and although some of the standard tests have been greatly simplified by the invention of the flame photometer (Barnes *et al.*, 1945), it was difficult to fit this extra work into the laboratory routine of a busy hospital. In the United States special metabolic research laboratories have been set up for this purpose. Even so we noted that Moore and Ball and their numerous collaborators required three years to study thirty adult cases – by far the largest study yet attempted. Most other detailed metabolic investigations, especially those concerned with infants, deal with only a few cases – often no more than two or three. It is difficult to see how this situation could be remedied unless armies of investigators could be raised – a practical, and especially a financial, impossibility.

Therefore, two considerations must be kept in mind. One is that the number of cases investigated is probably too small to be statistically significant. For this reason it must be clearly understood that in discussing the results of our experiments and in trying to deduce some generalizations, our report deals only with trends and cannot be dogmatic about any single finding. The other consideration concerns the fact that many surgeons have neither the facilities nor the time to perform extensive metabolic studies on their patients. Throughout our investigations we were aware that unless our studies helped us to evolve a pre- and post-operative régime that was as satisfactory from the clinical as from the laboratory point of view, we had, at best, been engaged in an academic exercise. In the last chapter of this report we have therefore attempted to correlate the laboratory findings with the clinical opinions and have described the pre- and post-operative régime that seems indicated.

Whilst we have studied in detail only nine patients during our metabolic investigations, our clinical experience over a five-year period comprises more than three hundred neonates suffering from urgent surgical conditions. As a result of the pre- and post-operative régime established in accordance with the findings of our study, the mortality for major surgical procedures on neonates fell from 76 per cent in 1949 (Rickham, 1952) to about 25 per cent in 1952, and is still falling. The mortality rate for neonates with intestinal obstruction alone has fallen from 78 per cent in 1949 to 26 percent in 1952 (Forshall and Rickham, 1953). Although perfection of the anaesthesia used for neonatal surgery is undoubtedly partly responsible, we are convinced that the chief cause of the decrease in operative mortality has been the improvement of pre- and post-operative management. It is

CHAPTER II

Subjects and Methods

SELECTION OF PATIENTS

All the patients studied in this investiga tion were admitted to the Neonatal Surgical Unit at Alder Hey Childrens Hospital, Liverpool.

Age

All patients were under four weeks of age. Most of them were only a few days old. On the basis of clinical experience we had formed the opinion that there is a distinct difference in response to major surgical procedures between infants a few days old and those over two weeks old. We therefore in cluded three infants three weeks old in this investigation in order to compare the labora tory data.

Prematurity

Since the metabolism of premature infants has been the subject of many studies during recent years, it would have been of great interest to investigate the metabolic response of such infants to surgical procedures. We felt, however that the added risk of prematurity to infants undergoing extensive operations made it inadvisable to carry out our studies on infants of this age group, as any further interference with them might turn the scales against survival. None of the infants studied by us was therefore grossly premature, the smallest (Esther O) weighing 1 902 gm. However, metabolic studies carried out by other investigators on premature babies and certain clinical impressions of our own do make it possible to discuss some aspects of the premature infant s met abolic response to surgery

Sex

With one exception (Esther O) the pa tients have been boys This selection was made because of the great difficulty in collecting all urine passed by baby girls without resort to continuous catheterisation.

Types of Cases

The patients were selected according to the following criteria

1 To study the effect of operative trauma alone, on infants who had been fed pre-operatively and whose fluid and electrolyte balances were undisturbed – i.e., ex cision of tumours from otherwise normal babies (3 cases)
2. To study the effect of operative trauma upon babies who had had no previous fluid and food intake and had had no abnormal losses – i.e., operations on infants with oesophageal atresia (2 cases)



FIGURE 2. (*right*) To facilitate the collection of faeces the infant is nursed on a rubber sheet throughout the period of investigation. Urine is collected in a sterile bottle as shown Wound discharge is minimized by sealing the opening with plastic glue. Vomiting is prevented by continuous gastric suction. Intra venous infusion is given by way of a scalp vein the needle being fixed to the scalp with plaster of Paris.

FIGURE 1 (*left*) Measuring burette of 30 ml capacity (accurate to 1 ml) which is routinely employed for all neonates receiving intravenous infusion

longed periods. It was eventually found that a short length of Paul's colostomy tubing, which can be obtained in a variety of diameters, could be pulled over any size of penis, fixed with strapping, and connected to a receiving bottle. This method is practically fool-proof, and if a new piece of tubing is applied each day, there is no leak and the infant's skin does not become inflamed (Edmunds, 1950).

VOMITUS. Vomiting is very common in infants with surgical conditions, but collection of the vomitus presents a difficult problem. In order to prevent vomiting, infants operated upon for intestinal obstruction were kept on continuous post-operative gastric suction. However, if the baby vomited in spite of all precautions, the nurse immediately sucked up the vomitus with pipettes and stored it in glass containers in the refrigerator. As no materials were used which could absorb the spilled fluid, it was comparatively easy to suck up the vomitus from the baby's skin or the rubber sheeting.

Urine, faeces, and aspirations were stored in the refrigerator and "pooled" every twenty-four hours for analysis.

WOUND DISCHARGE. To prevent discharge, the wounds were sealed off with a quick-drying elastic plastic glue (Portex). We thus circumvented the difficulty that other investigators had experienced in collecting wound discharges from absorptive dressings.*

INSENSIBLE WATER LOSS. Losses of water and electrolytes through the skin are hard to determine with any accuracy and have therefore been ignored in many balance studies. Water losses can be estimated to a certain extent from the weight changes, but the loss of electrolytes can only be measured with great difficulty (Gamble *et al.*, 1951). Burch and Winsor (1945) found that adult males lost 20.5 gm of water hourly per square meter of body surface. Darrow (1948) estimated that the imperceptible water loss from lungs and skin was 44 gm for every 100 calories metabolized, and Darrow *et al.* (1948) computed that this water loss in infants was between 50 and 100 ml per kg of body weight. Pointing out that infants lose a lot of insensible water because of the relatively large surface area of their bodies, Butler and Talbot (1944) computed that the daily loss of an infant weighing from 2 to 10 kg would range from 75 to 300 gm. They also stated that the insensible water loss increases by 100 per cent after operation. On the other hand, O'Brien *et al.* (1954) estimated accurately the insensible water loss of newborn infants nursed at a constant temperature of 31° C. in a supersaturated atmosphere of water mist – i.e., under conditions identical with those of the incubators in which our babies were nursed. Under these circumstances, the daily total insensible water loss was 13.8 gm per kg of body weight, 3.8 gm represented water lost from the lungs and 10 gm water lost from the body surface. This total was not quite half the amount of insensible water lost by babies nursed in room air. As Darrow pointed out in 1950 the only way to prevent inaccuracies due to insensible water loss in metabolic balance studies on infants is to nurse them at a constant temperature of 80° to 82° F in an atmosphere of constant high humidity. Happily, our routine method of nursing neonates post-operatively in incubators closely follows the criteria laid down by Darrow.

In discussing the loss of electrolytes through the skin Conn (1949) estimated that sweat contains between 15 and 60 meq of sodium chloride per litre. However, the sodium chloride content of infants' sweat is much lower than adults (Cooke *et al.*, 1950). An infant weighing 2.5 kg loses only 0.21 mM of chloride per day (Swanson and Iob, 1933).

* There was one exception. The wound of Case 2 was covered by absorptive dressing and a certain amount of wound leakage occurred.

with 0.2 ml of the one-in-ten plasma dilution. The final back titration was carried out with a 0.5 ml micro-burette (Agla micrometer syringe)

7 Plasma sodium and potassium were estimated by flame photometry, using 0.2 ml and 1.0 ml, respectively of the one-in-ten plasma dilution.

8 The plasma carbon dioxide saturation capacity was determined with a micro-manometric gasometer of the Natelson type (1951), using 0 03 ml of plasma.

9 The lower layer of plasma and the upper layer of cells were drawn off by a Pasteur pipette and used to determine blood urea concentration (from 0 05 to 0 1 ml, according to the amount available) by direct nesslerization of protein free filtrate after incubating with urease (micro modification of King, 1951)

10 The remaining cells were then packed by spinning for half an hour at 3,000 r p.m The rest of the plasma and the whole top layer of cells were then drawn off and used to increase the amount available for urea estimation (item 9 above) The lower layer of packed cells was then drawn up to the mark in a 0.2 ml pipette, the outside of the pipette carefully wiped, and the cells expelled into 1.8 ml of glass-distilled water After ten minutes the tube was spun and the supernatant fluid transferred to a clean dry tube. Aliquots of the one-in-ten dilution of cells were then used (after further dilution where necessary) to determine the sodium, chloride, and potassium contents of cells by methods similar to those detailed above.

11 The haemoglobin content of the whole blood was estimated with a M.R.C. grey wedge photometer (King *et al.*, 1948)

12. Eosinophil counts were made in order to study the changes in adreno-corticoid function of neonates undergoing operations We used the stain introduced by Randolph (1949), Phloxine and methylene blue dissolved in equal parts of propylene glycol and water, for counting the eosinophils in the chamber Eosinophil counts in normal newborn infants vary widely According to Klein and Hanson (1950), the range for 30 infants on the first day of life was 78 to 288, the range for 33 infants on the second day of life was 75 to 1,100, and the average range for these two days was 359 ± 47 and 420 ± 43, respectively

Estimation of Body Fluids

Although determination of the metabolic balance during the post-operative period was the primary object of our investigation, we thought that pre-operative data on the plasma, extra-cellular fluid, and total body water volumes would also be useful. Techniques that would be applicable to capillary blood samples were therefore elaborated, but as we considered that they carried some risk to the infants, they were not performed in all cases, nor did we repeat them in the post-operative period. Furthermore, we did not consider it justifiable to subject normal infants to unnecessary manipulations in order to obtain control values For these reasons the determinations of plasma, extra-cellular fluid, and total body water volumes, although of considerable interest, are not submitted as an integral part of the investigation. The techniques that we employed are described below

BLOOD VOLUME. Estimation of plasma volume has been commonly carried out with T.1824 (Evans Blue) Other dyes such as Vital Red (Keith *et al.*, 1915) and, more recently Blue Geigy 536 (Weiss *et al.*, 1953) have also been used, but their efficacy is not yet generally accepted.

A micro version of the Evans Blue method

fluid volume. We used the thiosulphate technique of Cardozo and Edelman (1952), modified as follows

A sterile 10 per cent solution of sodium thiosulphate containing a little Evans Blue was prepared. Approximately 4.5 ml of this solution was introduced through the drip tube, in a manner similar to that described above, as soon as the second fontanelle sample had been taken. The actual amount injected was determined by weighing the syringe and needle before and after injection, and also weighing an accurately measured volume of the solution. The latter was used to make up the standard solutions required in the subsequent analysis of plasma specimens. The coloured thiosulphate solution was injected at a steady rate, over a period of about 10 minutes, and then flushed through with 2 or 3 ml of glucose water The added dye indicated when the polythene tube was clear of the thiosulphate solution. Five capillary blood samples of heparinized blood were taken at 10-minute intervals over a period of 20 to 70 minutes after the start of the injection.

TOTAL BODY WATER VOLUME. This can be measured either by isotope dilution (F D Moore, 1946, Schloerb *et al.* 1950) or by intravenous injection of antipyrine (Davies, 1937) Antipyrine is, however not considered to be an ideal agent for the measurement of total body water, as it is bound to plasma proteins to the extent of about 10 per cent. N-acetyl-4-amino-antipyrine (NAAP) was found by Brodie and Axelrod (1950) to be distributed in the tissues in proportion to their water content, being *negligibly bound* to proteins and not metabolized to any appreciable degree. This substance was used by Brodie *et al.* (1951) in estimating the total body water, and we adopted their methods with some modifications.

A few minutes after the completion of the thiosulphate injection 2 ml of a sterile, coloured solution containing 0 04 gm of NAAP was injected by similar technique over a 5-minute period. The drip was run at a maximum rate of 5 ml per hour during the ensuing 6 hours, and heparinized capillary blood samples were taken at 3, 4½, and 6 hours. Using 0.2 ml instead of 2 ml plasma samples, we analysed these by the technique of Brodie *et al* (1951)

The results obtained by the above three techniques were corrected for the amounts of fluid injected and removed during the tests

A good basis for comparison was afforded by the extensive studies of Friis-Hansen and his colleagues Using deuterium oxide and antipyrine, Friis Hansen *et al.* (1951) found that the total body water of premature and full term neonates was between 70.2 and 83 per cent of the total body weight, and Edelman *et al.* (1952) determined that the proportion was 76 7 per cent. The same investigators found a relationship of 12.1 L/m^2 between total body water and body surface.

PRESENTATION AND CHARTING

Balance Charts

Accurate balance data were compiled in tabular form, but have not been included in the present report. Whilst these data are the exact results of our investigations, they are difficult to comprehend and to visualize. A much more comprehensible, although slightly less accurate, representation can be achieved by graphic means (see Charts 1–9)

Numerous methods of charting have been used by different investigators. We have used a slight modification of the method described by Moore and Ball (1952) not only because this method served our purposes well but also because the pattern of our research closely followed that of the Boston investigators, although concerned with newborn infants rather than adult patients.

The daily nitrogen, chloride, sodium, and

CHAPTER III

Investigation and Results

Introductory Note

As stated in Chapter II, the patients studied in this investigation were admitted to the Neonatal Surgical Unit at Alder Hey Children's Hospital, Liverpool.

Throughout their stay in the hospital, the infants were nursed in incubators in which the oxygen content of the atmosphere was kept at 50 per cent, the humidity at 100 per cent, and the temperature at 85°F One infant (Case 6) was nursed at a temperature of 90°F During operation the infants were not protected against heat loss in any way, and their body temperature often dropped quite considerably They were returned to the incubator immediately after operation.

Antibiotic therapy was routinely instituted before operation. In each case penicillin (250 000 units daily) and streptomycin (150 mg daily) were given parenterally Cases 4 and 7 received additional antibiotic therapy

An intravenous infusion was set up preoperatively, and, except in Cases 4 and 5 continuous gastric suction was started pre-operatively to prevent vomiting.

In each case, sedation was accomplished by atropine (1/400 gr), and anaesthesia was induced by endotracheal administration of oxygen and nitrous oxide, with minimal ether Succinylcholine was given intravenously

CASE 1 (GEORGE S)

History

23rd May 1953 DATE OF BIRTH

23rd May 1953 ADMITTED TO THE NEONATAL SURGICAL UNIT

WEIGHT 2,916 gm.

DIAGNOSIS Exomphalos.

EXAMINATION The infant's general condition was satisfactory Hydration was adequate. A loop of intestine could be seen through the thin membrane covering the exomphalos (diam. about 1 in.)

24th May 1953 OPERATION (time 1 hour) The exomphalos was found to contain a large Meckel's diverticulum, which was resected.

25th May 1953 The child's condition was very good. Intravenous infusion was discontinued, and oral feeding with glucose saline was started. Gastric suction stopped.

26th May 1953 Condition stationary; feeding with half-strength milk mixture started.

27th May 1953 First milk stools passed.

28th May 1953 Feeding with full-strength mixture started. Antibiotics stopped.

31st May 1953 Child very well, stitches removed.

13th June 1953. Child very well and gaining satisfactorily, discharged home.

of keeping newborn infants cool during operation (see Chapter IV, p 66) No artificial methods of cooling were employed, but we did not take precautions against loss of heat, by the use of clothing, blankets, hot water bottles, etc.

WEIGHT The birth weight was slightly below average and dropped by 100 gm after operation. It then remained practically steady, and during the first week after operation there was a net gain of 56 gm. This is interesting in view of the fact that most infants lose between 5 and 10 per cent of their weight during the first five days of life (Young *et al.*, 1950)

EOSINOPHIL COUNT On the day of operation the eosinophil count was 297/mm³, which is within normal limits. Following operation the count dropped steadily until the sixth day of the study, when a slight rise occurred. On the seventh and eighth days values below 50/mm³ were recorded. The decrease continued while the child was making an uninterrupted recovery

FLUID BALANCE. The fluid intake, rising from 128 ml on the first day to 480 ml on the fifth day, was more than adequate for a child less than one week old. Practically the whole fluid intake on the first day and 42 ml of the intake on the second day consisted of intravenously infused 5 per cent glucose saline The urinary output was only 7 ml on the day of operation — almost all the water being retained. It is difficult to decide whether the very low urinary output should be attributed to primary water retention, which Le Quesne (1954a, b) observed post-operatively in adults, or to the fact that infants secrete very little during the first few days of life — 20 ml being given by Thomson (1944) as an average for the first two days. The urinary and hence the total fluid output was within normal limits, except during the first three days after operation, when it was rather higher than the values recorded for normal full-term infants by Thomson (1944) It must, however, be added that the neonates in Thomson's study had, on the whole, a lower fluid intake than the baby under discussion.

Except on the second day, when only about 30 per cent of the fluid intake was retained, the percentage of water retained was rather greater than the normal values given by Thomson. Thereafter, the amount of water retained remained fairly constant, between 200 and 340 ml. This would explain the absence of the usual post natal drop in weight.

CALORIES. The caloric intake rose steadily from around 20 calories on the first day to roughly 200 calories from the fifth day onwards. This caloric intake was somewhat lower than the 80 calories per kilogram of body weight usually allowed for full term babies (Smith, 1951), but it was adequate for the immediate post-operative period.

NITROGEN BALANCE. During the first two days of our study the nitrogen intake was nil. The nitrogen output was very small on the first day but was greatly increased during the second day — 520 mg being excreted, 425 mg in the urine. The urinary nitrogen concentration was 354 mg per cent. This concentration was considerably higher than that found during the following week but still below the average (exceeding 700 ml per cent) found in normal infants urine at similar ages (Barlow and McCance, 1948) The low concentration during the following week can be explained by the relatively large fluid output.

As stated above, a relatively large amount of nitrogen was excreted on the second day in spite of a zero intake. From then onwards, with increasing intake, the positive balance became rapidly larger From the fifth day onwards, roughly between 700 and 1,000 mg of nitrogen *were retained* each day — or from 230 to 330 mg per kg of body weight, which is considerably higher than the daily average of 160 mg per kg of body weight retained by breast fed infants during the first month of life (Beach *et al.*, 1941) According to Moore

and Hoffman *et al.* (1949), for premature babies, noticed a retention of potassium greatly in excess of that required for the formation of normal tissues Wallace (1952) estimated the K N ratio in normal infants to be between 4.1 and 6.8 meq/gm.

Blood Studies (Table 1)

PLASMA ALKALI RESERVE AND CHLORIDE LEVEL. Throughout the whole period of observation, the alkali reserve was remarkably low There was a steady increase in the acidosis after operation and only on the sixth day was there a slight upward trend of the curve. As was to be expected, the plasma chloride level was very high, except on the fifth and sixth days, when it was below normal.

It has been known for some time that normal infants often develop acidosis with high plasma chloride levels Branning (1942) reported the average level of plasma bicarbonate for premature infants to be 16.8 meq/L. Young *et al.* (1941) found that the chloride level in premature infants between 8 and 18 days old was 109 meq/L, and Darrow (1946) found that it might rise to a maximum of 114 meq/L, unless the infants were fed with sodium bicarbonate.

The plasma alkali reserve in the infant under discussion was slightly below the figures quoted above As has been noted before (Hoffman *et al.*, 1949), there was no clinical evidence of acidosis. The infant was very well and apparently thriving The acidosis and hyperchloraemia subsided very slowly, but blood tests performed three months later showed that the blood chemistry had returned to normal. There is little doubt that the acidosis was produced by retention of chloride in excess of sodium, as in cases previously reported by Darrow (1946)

PLASMA SODIUM AND POTASSIUM LEVELS The plasma sodium concentrations were well

Table 1. Blood, Body Fluids, and Other Data

Day	1st	2nd	3rd	4th	5th	6th	7th	8th	9th	10th	95th
Hb. gm %	23.5	22.0	23.1	–	20.8	18.8	19.5	19.2	–	–	–
Hct. % cells	–	64.5	66.1	64 1	58.2	56 7	–	–	–	–	–
Blood urea mg %	27	50	34	32	36	34	35	–	42	–	18
P alk. res. meq/L	16.7	13.3	13.5	11 7	11 7	13	13 6	–	14	–	20
P Cl meq/L	104	107	116	118	89	95.3	109 7	–	134	–	93
P Na meq/L	138	144	152	144	123	130	143	–	158	–	–
P K meq/L	8.8	4.7	6.7	6.1	5.6	5 4	5 1	–	5.3	–	5 78
P prot. gm %	–	6.5	7 6	6.65	6 0	5.65	5 95	–	8.2	–	6 0
Cell N_2 gm %	–	9.1	9 0	7.8	7.5	10.2	10 4	–	–	–	–
Cell Cl meq/L	–	60	54.8	46.8	47.2	64 7	79 0	–	49.2	–	–
Cell Na meq/L	–	22.7	23.2	16 7	24.8	22.0	31.3	–	50	–	–
Cell K meq/L	–	84.1	90.5	79 0	80 0	79.5	82.5	–	79.5	–	–
Weight (gm)	2,916	–	2,820	2,824	2,826	2,839	2,839	2,869	2,876	2,863	–
Eos. per mm^3	297	220	206	–	107	138	34	43	–	–	–
PV (ml)	–	–	–	–	–	–	–	–	–	–	–
ECF (ml)	–	–	–	–	–	–	–	–	–	–	–
TBW (ml)	–	–	–	–	–	–	–	–	–	–	–

CASE 2 (CHRISTOPHER B)

History

21st October 1953 DATE OF BIRTH

11th November 1953 ADMITTED TO THE NEONATAL SURGICAL UNIT

WEIGHT 3,880 gm.

DIAGNOSIS Cystic hygroma of right axilla.

HISTORY The child was born by a difficult forceps delivery He suffered from haemorrhagic disease of the newborn and had been treated with vitamin K and blood transfusions A swelling in the right axilla was noticed at birth and had since increased in size

EXAMINATION The infant s general condition and colour were good. The haemoglobin concentration was 10 9 gm per cent. There was a very large, cystic, multilocular swelling over the right side of the chest, extending to the right axilla and the right side of the neck.

14th November 1953 OPERATION (time 1 hour, 30 minutes) When the hygroma was dissected out, it was found to extend underneath the right pectoralis major and minor, which had to be divided. The tumour was closely adherent to the axillary vessels and had to be dissected off the vessels and nerves.

15th November 1953 The child's general condition was good. The intravenous infusion and gastric suction were discontinued and oral feeding with glucose water, and later with half-strength milk mixture, was started.

18th November 1953 Some oedema was noted over the right deltoid and a pressure dressing was applied. Feeding with full strength milk mixture was started. Anti biotics stopped.

25th November 1953 Wound healed, stitches removed.

3rd December 1953 Child very well, discharged home.

Balance Study (Chart 2 and Table 2)

This study was undertaken in order to investigate the metabolic response of an infant undergoing operation for cystic hygroma at the age of about three weeks. Shortly after birth the infant had been given blood transfusions to counteract anaemia resulting from haemorrhagic disease, but prior to operation he had been well for over two weeks and steadily gaining weight on adequate milk feeds As the cystic hygroma was very large, the operation was of considerable magnitude and resulted in a blood loss of over 70 ml. Convalescence was rapid and successful.

TEMPERATURE. The temperature was normal, except on the third day, when there was a slight pyrexia, but this rapidly subsided.

WEIGHT The patient was a big baby There was a weight loss of over 250 gm on the first post-operative day The tumour contained a large amount of fluid, which could not be adequately measured during operation, and its removal was undoubtedly the main cause of weight loss. Unfortunately, because of some leakage from the wound, it was impossible to weigh the infant without dressings, except on the fourth day and on the day following cessation of the study

EOSINOPHIL COUNT The eosinophil count was much higher initially than in Case 1 It dropped to practically zero two days after operation and then gradually rose to a level above the pre-operative figure. The response closely resembled that reported for adults following operative trauma (Laragh and Almy, 1948)

FLUID BALANCE. The fluid intake was adequate, throughout the investigation, 268 ml of fluid were given intravenously during the first day 78 ml during the second day The urinary output was high, even on the day of operation, and the size of the positive fluid balance was very similar to that found in Case 1, who was considerably younger and smaller

values were about the same as those expected in normal babies. On the fifth and sixth days the sodium balances were almost zero The absence of early sodium retention and the relatively small late retention were unusual, but similar atypical findings have been reported for adults (Moore and Ball, 1952)

POTASSIUM BALANCE. It was in the potassium balance that Case 2 differed most obviously from Case 1 In spite of the high potassium intake, the balance was continuously and markedly negative throughout the six days of the study, except on the third day, when a minimal positive balance accompanied a very large intake. The infant therefore closely resembled an adult undergoing extensive surgery In the absence of vomiting and diarrhoea the potassium losses were truly formidable. Surprisingly, the faecal losses were nearly as great as the urinary losses.

THE K N RATIO During the first two days, when the nitrogen and potassium balances were both negative, the *K N ratio* was 7.2 meq/gm, which was considerably in excess of the K N ratio associated with breakdown of lean muscle tissue. Here again the values differed from those found in Case 1 and resembled those found in adults. Because the two balances had different signs from the third day onwards, it was impossible to calculate the K N ratio for the succeeding days

Blood Studies (Table 2)

PLASMA CHLORIDE AND SODIUM LEVELS. These were more or less normal and showed only insignificant changes.

PLASMA POTASSIUM LEVELS The plasma potassium concentrations showed wide variations. Twice, on the third and fifth days,

Table 2. Blood, Body Fluids, and Other Data

Day	*1st*	*2nd*	*3rd*	*4th*	*5th*	*6th*	*7th*
Hb. gm %	12	11.5	14.2	11.2	11.8	11.8	12.8
Hct. % cells	82.8	–	85.8	36.9	85 7	36.2	36.0
Blood urea mg %	16	–	60	40	43	40	54
P alk. res. meq/L	22	–	21.5	20 4	19 1	23.1	25.0
P Cl meq/L	104	–	102.5	104	98	93.6	98.8
P Na meq/L	143	–	140	141	136	130	188
P K meq/L	4	–	6	4.4	6	4	4.7
P prot. gm %	5 7	–	7	6.75	6.5	5.25	5.2
Cell N gm %	6.75	–	–	5.8	4.75	5 7	4.9
Cell Cl meq/L	75	–	70	64.3	48.4	48.4	48.4
Cell Na meq/L	12	–	17	19	10	12	83
Cell K meq/L	92.8	–	90	98.7	89	83.8	73.8
Weight (gm)	3,880	3,621	–	8,832	–	–	–
Eos. per mm³	657	–	16	246	849	680	858
PV (ml)	249	–	–	–	–	–	
ECF (ml)	1,625	–	–	–	–	–	
TBW (ml)	2,955	–	–	–	–	–	

iod of potassium depletion would pre-
ably have been followed by potassium
ention to make up for post-operative losses.
assium loss accompanied by sodium gain
found in the red blood corpuscles.

The chloride and sodium balances were
er atypical, as the early retention was
ent and late retention was not very
rked.

This infant, then, showed nitrogen and
ctrolyte balances as well as an eosinophil
ponse rather different from those found
Case 1 and very similar to those found in
lt patients.

CASE 3 (JOHN D)

History

h August 1954 DATE OF BIRTH

h September 1954 ADMITTED TO THE NEONATAL SURGICAL UNIT

WEIGHT 3,774 gm.

DIAGNOSIS Meningocele.

EXAMINATION The child's general condition was good. A small, lumbar meningocele, with a very thin membrane covering it, was noted. There was no paralysis and no hydrocephalus.

th September 1954 OPERATION (time 35 minutes) When the meningocele was excised it was found to have only a very narrow communication with the spinal theca. The narrow stalk was ligated. Post operatively the intravenous infusion and gastric suction were discontinued and oral feeding with glucose water was started.

th September 1954 The child's condition was very good. Oral feeding with milk mixtures was started. In order to prevent any vomiting, the stomach was aspirated before each feeding

The child continued to make a satisfactory recovery during the next few days.

1st September 1954 Wound healed, stitches removed. Antibiotics stopped.

5th September 1954 Child discharged home.

Balance Study (Chart 3 and Table 3)

It was thought that the difference in the metabolic response between Case 1 and Case 2 might have been due, not to the difference in age, but to the fact that the magnitude of the operation in Case 2 was much greater than in Case 1 Consequently, it was decided to investigate the metabolic response to surgery of another three-week-old infant, who required a comparatively minor operation. As Case 3 had only a small meningocele, with a narrow stalk and no neurological involvement, the operation could be scheduled for a convenient time. He was therefore a good subject for this study He stood the operation well, and convalescence was uneventful.

TEMPERATURE The temperature remained slightly below normal during the whole period of observation. There were no wide variations.

WEIGHT The patient was a big baby There was a weight drop of 80 gm on the second day, which could not be accounted for by the amount of tissue removed, which weighed only 16 gm. As a considerable amount of water was retained during the first day, the weight loss must have been mainly due to tissue breakdown. On the basis of Lusk's (1906) coefficient (33 gm of whole tissue equals 1 gm of nitrogen), the amount of protein tissue lost was in the neighbourhood of 10 gm. The rest of the tissue broken down was presumably fat. By the third day the weight loss had been made good, and between the second day and seventh day there was an over all weight gain of more than 130 gm.

EOSINOPHIL COUNT On the first day the eosinophil count was unusually low for a baby of three weeks, but, as discussed before, there exist wide individual variations. The count dropped to a very low level on the second day After a sharp rise on the third day, it alternately rose and fell but never reached

and excretion were high, there was considerable retention.

POTASSIUM BALANCE. As in Case 2, the potassium excretion was very high In spite of considerable intake of potassium the balance was negative except on the second and sixth days During the seven-day period of observation only about 3 meq of potassium were retained. (In other words, there was a marked potassium excretion in spite of a very high potassium intake, nearly 90 per cent of the *potassium loss occurring in the urine*) The minimal potassium retention took place in the presence of a high nitrogen retention, about 7.5 gm of nitrogen being retained during the same period.

THE K N RATIO During the short negative phase on the day of operation, when no nitrogen or potassium was given, the K N ratio was 9.3 meq/gm – a figure greatly in excess of that found in lean muscle tissue During the remainder of the period the two daily balances usually had different signs, and it was therefore impossible to calculate the K N ratio on a daily basis. The over all potassium and nitrogen balances during the last six day were positive, and the K N ratio for this period was very low, approximately 0 9

Blood Studies (Table 3)

PLASMA ALKALI RESERVE AND CHLORIDE AND SODIUM LEVELS These were slightly elevated on the first day but remained more or less normal during the rest of the study

PLASMA POTASSIUM LEVEL. This remained within high normal limits.

OTHER BLOOD INVESTIGATIONS These were within normal limits for a three-week-old infant.

BODY FLUIDS The estimated plasma volume was 269.5 ml, but this figure is probably inaccurate, as it would correspond to 114 ml of blood per kg of body weight. The extracellular fluid volume was 1,543 ml, or 40.9 per cent of the body weight, and the total

Table 3. Blood, Body Fluids, and Other Data

Day	1st	2nd	3rd	4th	5th	6th	7th	8th
Hb gm %	16 9	16 3	14.5	15.3	13 1	12.6	13.5	–
Hct. % cells	45	49	40.5	40.8	43.5	42.1	40 7	40.2
Blood urea mg %	24	18	27	30	52	32	43	53
P alk. res. meq/L	24.6	22.7	16.8	19.8	21.5	21.2	20 6	21 9
P Cl meq/L	112.1	101.3	101	100	102.2	102.5	105.1	93.6
P Na meq/L	147	130	130	129	132	132	133	129
P K meq/L	5 0	4.9	4.9	4 9	4.7	4.8	5 4	5.2
P prot. gm %	6.05	6.55	6.65	5 9	6.2	6 45	6.25	6 4
Cell N, gm %	1.89	–	1.82	1 75	1 75	1 79	1.64	1.61
Cell Cl meq/L	51.2	57 4	57 4	57 7	50 0	55.5	53.1	50 1
Cell Na meq/L	18	33	25.5	22	21	31	23	21
Cell K meq/L	82.5	83	84.1	80	82	80	82.1	80
Weight (gm)	3 774	3,693	3,796	3,844	3,798	3,819	3,826	–
Eos. per mm³	147	14	106	94	139	52	63	–
PV (ml)	269.5	–	–	–	–	–	–	–
ECF (ml)	1,543	–	–	–	–	–	–	–
TBW (ml)	2,820	–	–	–	–	–	–	–

6th March 1953 Massive collapse of the right lung occurred. The right bronchus was sucked out and the lung re-expanded. An intravenous infusion was set up.

7th March 1953 Another tension pneumothorax developed, and an intercostal drain was inserted into the right pleural cavity

8th March 1953 The infant s condition was satisfactory The intravenous infusion was discontinued. Penicillin and streptomycin were discontinued. Aureomycin (20 mg) was given orally every six hours

9th March 1953 Oral feeding with glucose water was begun. However, the child had a sudden attack of cyanosis and dyspnoea. Resuscitation was of no avail, and the infant died soon after

POST MORTEM EXAMINATION There was found to be a leak from the oesophageal anastomosis, widespread bilateral bronchopneumonia with an early bilateral empyema was noted.

CAUSE OF DEATH Bronchopneumonia.

Balance Study (Chart 4 and Table 4)

This study was undertaken in order to investigate the metabolic response of a new born infant undergoing an extensive chest operation for oesophageal atresia. There had been no fluid or food intake prior to admission. In addition, the baby had had some respiratory distress before the study commenced. The initial post-operative period was satisfactory, but a mediastinal leak developed which finally led to the infant s death six days after operation.

TEMPERATURE. Throughout the investigation the temperature was subnormal, its lowest point being 90° F during operation. A subnormal body temperature in neonates undergoing surgery has been given a grave prognosis by some surgeons (Santulli, 1954) It is, however, our impression that young infants, like young animals, usually stand low body temperatures very well indeed (see also Churchill-Davidson *et al.*, 1953) It must be assumed that such a continuous low body temperature has some influence upon metabolism. It is, of course, known that the basal metabolic rate and the tissue oxygen requirements are diminished when the body temperature is lowered, but the effect of these conditions upon the nitrogen and electrolyte balances have, as yet, not been fully investigated.

WEIGHT The birth weight of just over 2,700 gm was considerably below average, although

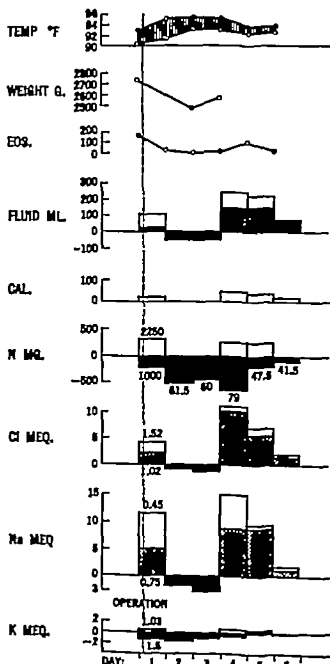


Chart 4. Metabolic Balance Data

first four days, the difference in the potassium balance being mainly due to varying amounts of potassium excreted in the stools.

THE K N RATIO During the seven-day period the K N ratio was 2.78 meq/gm, which is very close to the figure for lean muscle tissue. This suggests that during the operative and post-operative period the infant lost potassium at a rate corresponding to the break down of tissue protein The high post-opera tive K N ratio found in adults and older children was not reached. Excessive potassium loss did not occur, in spite of the very extensive, long, and shock producing surgical procedure and fatal post-operative complica tions.

Blood Studies (Table 4)

PLASMA ALKALI RESERVE. This was slightly lower than the normal range for infants of comparable age. It must be remembered that the patient received no milk feeds.

PLASMA SODIUM AND CHLORIDE LEVELS The curves ran parallel, rising above normal on the third day when the balance of these ions and water was negative, then dropping below normal on the fifth day at the time of maximum chloride, sodium, and water reten tion, and finally rising again to normal levels at the time of death. (The autopsy blood sample was taken by means of cardiac ventri cular puncture a few minutes after the child died.)

PLASMA POTASSIUM LEVEL. In general the curve followed the same trend as the sodium curve· it dropped below normal on the sixth day

OTHER BLOOD INVESTIGATIONS The blood urea rose steadily, except for a slight drop on

Table 4. Blood, Body Fluids, and Other Data

Day	1st	2nd	3rd	4th	5th	6th	7th P.M
Hb. gm %	22.9	24.6	20.5	21.4	22.7	24.8	–
Hct. % cells	63.2	72.1	74.2	64	71.4	66.6	64.2
Blood urea mg %	37	48	58	89	74	77	104
P alk. res meq/L	16.5	17 1	16 9	16.4	16 0	17 6	23 4
P Cl meq/L	103	106	109	103	92	94	104
P Na meq/L	130	141	149	130	125	128	137
P K meq/L	5.2	6.8	6.9	5 4	4.7	3.6	3.8
P prot. gm %	6.3	7.8	8.9	6.0	6.5	6.5	6.35
Cell N gm %	5 4	5.62	6	4.94	5.29	6.17	5.28
Cell Cl meq/L	49	90	–	57.5	67	75	66
Cell Na meq/L	41	15	15	2	1.5	2	2
Cell K meq/L	82.5	83.8	82.5	84.8	88.8	93.1	85.8
Weight (gm)	2,756.75	–	2,492	–	2,601.5	–	–
Eos. per mm³	175	40	19	26	118	44	–
PV (ml)	–	–	–	–	–	–	–
ECF (ml)	–	–	–	–	–	–	–
TBW (ml)	–	–	–	–	–	–	–

feeds well. There was some infection of the wound, and the infant's lips and left eye were inflamed. His penis had become inflamed from the continuous use of strapping to fix the rubber tube for collecting urine.

4th November 1953 The infant's general condition was good. There was still some skin infection. The metabolic balance experiment was stopped.

1st December 1953 The infant had been gaining steadily, and the wound had healed well. Although x ray examination with barium swallow did not show a stricture at the site of the anastomosis, there was a *slight* temporary hold up of the feeds at the anastomotic site. The child was discharged home.

Balance Study (Chart 5 and Table 5)

This study was undertaken in order to investigate the metabolic response of a newborn infant who was operated upon for oesophageal atresia. There were certain differences between this case and the preceding one. The infant under discussion was premature and was admitted when four days old, during which time he did not have any fluid or electrolyte intake. Clinically he was dehydrated, but not to a marked degree. Although the pre-operative conditions were therefore not favourable, this infant made an uninterrupted recovery

TEMPERATURE. The temperature remained normal or slightly below normal almost to the end of the investigation, which had to be discontinued because the infant developed multiple small skin infections.

WEIGHT The birth weight was reputed to be 5 lb., 6 oz. (2,440 gm) On admission the baby weighed 2,382 gm. Post-operatively he gained steadily and weighed 2,599 gm on the eighth day of the study

EOSINOPHIL COUNT The post-operative eosinophil count was surprisingly high (834/-

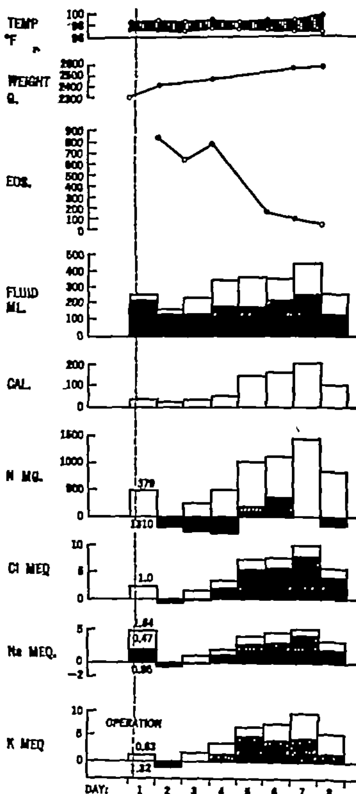


Chart 5. Metabolic Balance Data

mm³) Unfortunately, no count was performed before operation. Whilst the child was rapidly recovering the count fell continuously On the eighth day it was 83/mm³

infants over a three-day period (Hoffman *et al.*, 1949)

THE K N RATIO During the first two days, when the nitrogen and potassium balances were both negative, the K N ratio was 2.28 meq/gm. Again we see that this corresponds to the K N ratio of lean muscle tissue. Later on, retention of potassium was marked, whereas the nitrogen balance was nearly zero Potassium retention is difficult to ex plain, in the absence of previous excessive potassium loss, but it also occurs in premature infants who have not undergone operations (Hoffman *et al.*, 1949)

Blood Studies (Table 5)

PLASMA ALKALI RESERVE AND SODIUM AND CHLORIDE LEVELS. The alkali reserve rose to 19 8 meq on the fourth day and the plasma chloride level to 110 meq on the third day; thereafter both settled down to what we regard as normal for an infant of the premature age group

PLASMA SODIUM AND POTASSIUM LEVELS. The plasma sodium level, like the chloride level, showed a post-operative rise. On the sixth day the concentration fell to 125 meq, from the seventh day onwards it remained at 127 meq The potassium remained constantly between 5 05 and 5 3 meq/L, which is slightly higher than the range we have come to regard as normal for premature infants.

OTHER BLOOD INVESTIGATIONS The blood urea was over 120 mg per cent at the beginning of the study With increasing hydration it fell to normal levels. There was a slight upward trend on the eighth day, without any apparent cause.

The plasma protein concentration was also continuously above normal.

The haematocrit and haemoglobin levels, on the other hand, remained constantly be-

Table 5 Blood, Body Fluids, and Other Data

Day	1st	2nd	3rd	4th	5th	6th	7th	8th	9th
Hb gm %	19.2	15.3	15 7	14.8	–	14.8	14 7	–	–
Hct. % cells	–	–	48.8	45.9	45.9	46 1	46 1	–	40 7
Blood urea mg %	126	–	130	110	100	84	50	72	40
P alk. res. meq/L	16 7	–	19.3	19.8	17.1	15.0	17 1	19 1	19.1
P Cl meq/L	105	–	110	103	98	95	97	98	96.9
P Na meq/L	134	–	145	137	133	125	127	127	127
P K meq/L	5 05	–	5.1	5 1	5.07	5.07	5 1	5.3	5.3
P prot. gm %	6.9	–	9 4	6.9	7.2	6.6	6 7	5.9	5.9
Cell N gm %	7 76	–	5.2	5.04	5.32	6.0	6.72	–	5.68
Cell Cl meq/L	96.7	–	90	79	35	64	87	–	55
Cell Na meq/L	54	–	60	60	43.5	43	52	–	50
Cell K meq/L	84	–	77	73.7	71.6	82.4	115	–	97 1
Weight (gm)	2,382	2,450	–	2,496	–	–	2,589	2,599	–
Eos. per mm³	–	834	632	789	–	186	117	88	–
PV (ml)	244	–	–	–	–	–	–	–	–
ECF (ml)	820	–	–	–	–	–	–	–	–
TBW (ml)	1,536	–	–	–	–	–	–	–	–

On admission.

teristic features of a Mongol. She appeared to be mildly dehydrated. There was some epigastric distension and visible peristalsis was noted. X ray examination of the abdomen (with the child held in the upright position) showed typical duodenal obstruction. An indwelling catheter was passed into the bladder

31st January 1953 OPERATION (time 1 hour, 50 minutes) The abdomen was opened through a transverse supra umbilical incision. There was a small amount of free peritoneal fluid. Duodenal stenosis was found and a duodeno-jejunostomy was performed.

1st February 1953 The child's condition was satisfactory

2nd February 1953 The intravenous infusion was stopped and oral feeding with glucose water was started.

3rd February 1953 The child's general condition remained satisfactory There was some haematuria. Feeding with half strength Ostermilk no. 1 was started.

5th February 1953 The child's general condition was unchanged. There was some regurgitation of feeds and continued haematuria.

6th February 1953 The child had some respiratory distress and her general condition had deteriorated. Haematuria and regurgitation of feeds continued. An intravenous infusion was set up.

7th February 1953 The child's condition was very poor; she was cold and limp She died in the afternoon.

POST MORTEM EXAMINATION The larynx, trachea, and bronchi were found to contain blood-stained, frothy material. Both pleural cavities contained an excess of fluid and both lungs showed diffuse areas of consolidation. There was an excess of blood-stained fluid in the peritoneal cavity The stomach and the proximal part of the duodenum were dilated. There was a stenosis at the ampulla of Vater The duodeno-jejunostomy was patent and there was no leak. Some fatty degeneration of the liver was noted and the mucosa over the trigone of the bladder was haemorrhagic.

CAUSE OF DEATH Pneumonia and prematurity

Balance Study (Chart 6 and Table 6)

This study was undertaken in order to investigate the metabolic response of a premature infant undergoing a severe operation two days after birth. As the infant suffered from high intestinal obstruction, in addition to having been starved, she had lost a considerable quantity of fluid and electrolytes by copious vomiting during the two days before operation. Although her condition was fair immediately after operation, she soon developed bronchopneumonia, from which she died.

As has been mentioned before, this patient was the only girl in our series and she was a Mongol. Whilst we believe that the fact that she was a Mongol had little, if any, influence upon her metabolic response, it must be added that, in our experience, such babies die very frequently during the post-operative period, as they seem to be particularly susceptible to bronchopneumonia. Esther O was no exception in this respect, she had the additional disadvantage of being six weeks premature.

TEMPERATURE. The temperature was persistently subnormal, swinging between 84° and 86° F In our experience, this low body temperature is the rule with premature babies after operation.

WEIGHT The infant's birth weight was reputed to be 4 lb, 10 oz. (2,091 gm) On admission her weight was slightly over 1,900 gm. In spite of the fact that her condition was rapidly deteriorating during the post-operative period, she steadily gained weight

feeds. There was gradually increasing abdominal distension.

EXAMINATION The child's general condition was satisfactory Hydration was adequate. X ray examination of the abdomen (with the child held in the upright position) showed multiple fluid levels in the small intestine. X ray examination with barium enema showed typical Hirschsprung's disease the grossly dilated colon narrowed suddenly at the juncture of the descending and sigmoid sections of the colon.

7th May 1953 OPERATION (time 2 hours, 35 minutes) The abdomen was opened through a transverse infra umbilical incision. The splenic flexure, the descending and sigmoid sections of the colon, and the rectum were mobilized and a pull through recto-sigmoidectomy was performed.

8th May 1953 No bowel sounds. Urine passed.

9th May 1953 Meconium passed.

10th May 1953 The child looked pale. His tongue was swollen, and there was bleeding from the mouth. Oedema of the scalp and the extremities was noted. No bowel sounds were heard.

11th May 1953 The child's condition was poor His abdomen was distended but soft. No bowel sounds were heard. There was generalized oedema. There was bleeding from the mouth, and blood appeared in the urine. It was decided to discontinue penicillin and streptomycin. Terramycin (30 mg) was given intramuscularly every six hours.

12th May 1953: The child's condition was very poor He suddenly collapsed and died.

POST MORTEM EXAMINATION There was septicaemia, presumably secondary to a septic pylephlebitis of the right internal saphenous vein, which had been used for the first transfusion. Multiple abscesses in both lungs and an early bilateral empyema were found. The pharynx, oesophagus, and stomach showed multiple ulcerations. The other intra abdominal organs appeared normal and the operation site was soundly healed

CAUSE OF DEATH Septicaemia.

Balance Study (Chart 7 and Table 7)

In this study we investigated the metabolic response to surgery of a newborn infant suffering from low intestinal obstruction. Unlike Case 6, this infant was a full term baby As the obstruction was in the large intestine, the child had vomited only small amounts prior to admission and there were no clinical signs of dehydration. There was, however, gross abdominal distension, and although this distension was, in the main, due to gas, there must have been some accumulation of fluid in the intestine.

Although the child stood the very extensive operation quite well, he subsequently developed septic complications from which he died. Maximal trauma and maximal post-operative stress therefore, were involved in this case.

TEMPERATURE. Except on the first day, when there was a slight elevation, the temperature was normal or slightly subnormal, in spite of the septicaemia. In this respect the patient differed from the premature infant with high intestinal obstruction discussed previously

WEIGHT The birth weight was reputed to be 7½ lb (3,402 gm), but as in the previous cases, the accuracy of the birth weight is somewhat doubtful. On admission, the child weighed 3,150 gm. After operation he was given intravenous fluids continuously until his death, and it was therefore impossible to weigh him again.

EOSINOPHIL COUNT The eosinophil levels were extremely low throughout the period of investigation the lowest were reached the

considerably higher than the potassium concentration found in adult intestinal contents during ileus (Lesser and Pareira, 1953)

THE K N RATIO The K N ratio for the whole period of investigation was 2.86 meq/gm. This means that the potassium loss was not excessive, even though the balance remained negative and even though the child had vomited pre-operatively for three days, was subjected to severe operative stress, and died of its after-effects.

Blood Studies (Table 7)

PLASMA ALKALI RESERVE AND CHLORIDE LEVEL. The plasma alkali reserve was continuously above normal. The initial alkalosis was not surprising in view of the fact that the child had vomited pre-operatively During the post-operative period of continuous gastric suction, the aspirated material consisted mainly of mucus, the content of base slightly exceeding that of chloride. The plasma chloride concentration was also above normal, except on the fourth day

PLASMA SODIUM AND POTASSIUM LEVELS In general, these mirrored the chloride curves. But whilst the sodium curve continued to rise on the sixth day, the potassium level remained below normal.

OTHER BLOOD INVESTIGATIONS. Blood urea, plasma protein, and haematocrit levels were above normal at the beginning of the investigation, but the two latter curves fell below normal during the later part of the study

BODY FLUIDS On the first day the plasma volume was 178 ml. With a haematocrit reading of 49 per cent, the blood volume was calculated to amount to 310 ml, or 98 4 ml per kg of body weight. Figures for extra cellular fluid volume were not obtained for this patient.

The total body water volume was 2,016 ml, or over 60 per cent of the body weight. This figure, which is below the normal range for

Table 7 Blood, Body Fluids, and Other Data

Day	1st	2nd	3rd	4th	5th	6th
Hb. gm %	16.3	17.8	16.6	14.5	14.6	17.8
Hct. % cells	49	57	60.2	54.7	49.5	45 0
Blood urea mg %	66	41	38	43	56	54
P alk. res. meq/L	23.8	23.8	21.8	21.6	16.9	21.6
P Cl meq/L	103.5	111	110	89	101	114
P Na meq/L	141	158	145	128	136	144
P K meq/L	4 0	6.9	6.1	3.9	4.4	3 4
P prot. gm %	5.8	7 7	6.1	5 0	5.7	4.5
Cell N, gm %	–	4.6	4.5	4.15	5 6	5.35
Cell Cl meq/L	59.2	67 4	71.7	70.2	59.2	51.2
Cell Na meq/L	23.2	36 0	36.0	36.0	40.0	25 0
Cell K meq/L	100	100	54.6	81.0	87 0	94.3
Weight (gm)	3,150	–	–	–	–	–
Eos. per mm³	39	11	23	52	12	35
PV (ml)	178	–	–	–	–	–
ECF (ml)	–	–	–	–	–	–
TBW (ml)	2,016	–	–	–	–	–

the last twenty four hours the vomitus had become bile-stained.

EXAMINATION The child s general condition was fair He was moderately dehydrated. His abdomen was distended. X-ray examination showed multiple fluid levels in the small intestine. There was no air in the large intestine.

29th January 1954 OPERATION (time 40 minutes) The abdomen was opened through a transverse supra umbilical incision The jejunum and ilium were found to be dilated. There was a small ileo-ileal intussusception, which was easily reduced.

30th January 1954 No bowel sounds. No stool passed.

31st January 1954 Numerous bowel sounds were heard. Intravenous infusion and gastric suction were discontinued and oral feeding with glucose water was started. The infant passed a watery stool.

1st February 1954 Feeding with full-strength milk mixture started.

4th February 1954 Wound edges slightly inflamed.

7th February 1954 The infant was taking feeds well and gaining, wound was healed. Antibiotics stopped.

9th February 1954 Discharged home.

Balance Study (Chart 8 and Table 8)

This study was undertaken in order to observe the effect of an operation for intestinal obstruction upon an infant twenty five days old – i.e., considerably older than the two patients suffering from intestinal obstruction described in Cases 6 and 7 In the present case it is quite possible that the obstruction did not become complete until the last day, when the patient started to vomit bile. On admission the baby s general condition was quite good, and he was only mildly dehydrated. In this respect he differed from the two infants of similar age studied by Danowski *et al* (1950), as these patients had vomited for prolonged periods and were markedly dehydrated. Our patient also differed in that he had a low intestinal obstruction due to an intussusception, a very rare cause of obstruction in the neonatal age group (Koop 1953)

TEMPERATURE. This showed little variation. It was slightly below normal during the immediate post-operative period.

WEIGHT The infant weighed 2,426 gm on admission. By the third day, the weight had fallen to 2,209 gm it rose to 2,374 gm on the fourth day and then remained roughly stationary

EOSINOPHIL COUNT Unfortunately, a pre-operative count was not taken. On the second day the count was very low indeed. It rose to over 400/mm³ on the fourth day Slight drops occurred on the fifth and sixth days, coinciding with some inflammation of the wound.

FLUID BALANCE. The patient s fluid intake during the first four days was roughly half the amount theoretically required for a child of his age. During the first two days all fluids were given intravenously From the fifth day onwards there was an adequate fluid intake. The fluid output was somewhat diminished during the first two days, especially on the second day It then remained roughly constant until the last day of the study when an increased intake was accompanied by a reduced output. The relatively large positive fluid balance during the last four days may have indicated a certain amount of dehydration during the earlier periods of the investigation.

CALORIES. The caloric intake was inadequate during the first four days, but later it approached 80 calories per kg of body weight.

NITROGEN BALANCE. When the nitrogen intake was nil and the output small, the balance was negative. As soon as milk was given, the nitrogen balance became positive although the output increased. During the last four

Blood Studies (Table 8)

PLASMA ALKALI RESERVE AND CHLORIDE LEVEL. The plasma alkali reserve was slightly above normal at the start of the observation and the chloride concentration slightly below normal. This might well have been caused by preoperative vomiting Later on, the alkali reserve quickly fell to normal, there was marked chloride retention, and the plasma chloride level rose considerably

PLASMA SODIUM AND POTASSIUM LEVELS. The plasma sodium curve showed the same trend as the chloride curve, starting below normal and gradually reaching a normal level during the second part of the investigation. The same configuration can be observed when studying the plasma potassium curve. The hypokalaemic findings in the early post-operative period (e.g, 2.6 meq/L on the third day) resembled those reported by Danowski *et al.* (1950) for infants with pyloric stenosis but were at variance with our findings for the two younger infants with intestinal obstruction (Cases 6 and 7)

OTHER BLOOD INVESTIGATIONS Blood urea and plasma protein concentrations were normal. The haematocrit and haemoglobin levels were lower than in the preceding cases, as would be expected, considering the age of the patient. Neither of these findings was suggestive of marked dehydration, which is somewhat surprising in view of the history of pre-operative vomiting and the low fluid intake during the early post-operative period.

CELL ELECTROLYTE LEVELS. The red cell chloride content was normal, except during the last two days, when it was slightly increased.

The cell sodium level was persistently above normal but remained more or less constant. The cell potassium level was especially low on the first day and, as in the preceding

Table 8. Blood, Body Fluids, and Other Data

Day	1st	2nd	3rd	4th	5th	6th	7th	8th
Hb. gm %	15 4	12.8	12.8	13	13	11.5	11.2	11.8
Hct. % cells	41 4	46.6	38.9	40 9	36.8	39.2	40 4	42.0
Blood urea mg %	24	28	24	17	17	22	26	28
P alk. res. meq/L	21.7	18.9	21.1	17 4	20 4	17 4	17 4	17.3
P Cl meq/L	93.1	99 1	93.1	104.3	100 0	102.5	110.3	115.9
P Na meq/L	131	128	133	128	130	131	136	139
P K meq/L	3 4	3.0	2.6	2.9	2.9	3.8	4.3	4.3
P prot. gm %	5.8	5.8	5.4	4.7	4.1	5 0	5.4	5.6
Cell N_2 gm %	5 7	5.1	4.9	5.7	4.1	4.8	5.2	4.8
Cell Cl meq/L	52.6	63.0	55 7	57 7	55.7	55.5	70.1	68.1
Cell Na meq/L	35.2	29.8	36.8	39.6	24 0	27.2	46 4	30.6
Cell K meq/L	67 7	81.3	76.7	79 0	83.9	83 1	84.4	91.2
Weight (gm)	2,426	–	2,209	2,374	2,362	2,355	2,360	2,338.5
Eos. per mm^3	–	87	181	402	245	183	516	303
PV (ml)	–	–	–	–	–	–	–	–
ECF (ml)	–	–	–	–	–	–	–	–
TBW (ml)	–	–	–	–	–	–	–	–

2nd February 1954 The intravenous infusion was continued. Oral feeding was tried again, but had to be discontinued because of vomiting X ray examination of the abdomen showed no air beyond the duodenum.

2nd February 1954 SECOND OPERATION (time 1 hour) When the abdomen was reopened, the anastomosis was found to be intact, but the bowel was kinked and obstructed by numerous adhesions The adhesions were divided and the gut was straightened.

3rd February 1954 The intravenous infusion was continued. Bile-stained fluid was continuously aspirated from the stomach.

4th February 1954 There were numerous bowel sounds, the bowel opened. The intravenous infusion was discontinued and oral feeding with glucose water was started.

5th February 1954 Considerable quantities of bile-stained fluid were again aspirated from the stomach. The intravenous infusion was set up again.

6th February 1954 Only small amounts of fluid were aspirated from the stomach. The intravenous infusion was stopped and oral feeding with diluted milk mixture was begun.

7th February 1954 There was still some vomiting The feedings were increased.

8th February 1954 No change child still vomiting Stomach was washed out.

9th February 1954 General condition improved, no vomiting Antibiotics stopped.

10th February 1954 Again copious vomiting. Oral feeding was continued but stomach was aspirated periodically

11th February 1954 The child had repeated tetanic convulsions. An intravenous infusion was started again and ammonium chloride was given intravenously

12th February 1954 The child had further attacks of tetany More ammonium chloride was given intravenously

13th February 1954 No more tetany The child was taking feeds well. Calcium gluconate was given intramuscularly

14th February 1954 The child was well and taking his feeds well. There was slight regurgitation. Intravenous infusion stopped.

16th February 1954 The child s general condition was good. A blood transfusion was given.

SUBSEQUENT COURSE: The child s general condition remained satisfactory, but he developed an obstructive jaundice A third operation was performed on 15th March 1954 to relieve the jaundice At operation it was found that the common bile duct was obstructed by numerous fibrous adhesions. A cholecysto-duodenostomy was performed Following this operation the jaundice quickly disappeared. The child improved steadily and was discharged on 29th March 1954.

Balance Study (Chart 9 and Table 9)

The study was undertaken in order to observe the metabolic response of another infant operated upon for intestinal obstruction a few days after birth. After an apparently satisfactory recovery, the child again developed a mechanical obstruction on the third post-operative day

Treatment by gastric suction and intravenous infusion was of no avail, and a second operation had to be performed five days after the first, in order to relieve this obstruction. The infant s condition was fair before the first operation but poor before the second one.

The metabolic study was continued. It now developed into a study of the effects of repeated operative trauma upon a newborn infant. Following the second operation there developed a period of intestinal ileus necessitating prolonged gastric suction and intravenous therapy Even when oral feeding was commenced, the infant s general condition did

not improve, and, to our surprise, he devel oped severe metabolic disturbances culmi nating in attacks of tetany lasting for nearly forty-eight hours after milk feeds had been started. As the child's life was endangered, we attempted to relieve the attacks by intravenous ammonium chloride. In spite of many technical difficulties, we were able to continue our balance studies throughout this period, until the baby s clinical condition and blood chemistry had ceased to give cause for anxiety Altogether, we proceeded with the balance studies for nineteen days and were thus able to record the metabolic changes fol lowing repeated trauma, as well as electrolyte depletion of great severity

In retrospect, it may seem surprising that this child should have survived the ordeal. The case gave further proof, if proof were needed, of the astonishing stamina of newborn infants. It also provided us with a mass of most useful data. The infant s subsequent development of jaundice, which had to be treated by yet a third operation, did not ma terially affect our study as the jaundice did not appear until after the investigation had been completed.

TEMPERATURE. In general, the temperature was normal or slightly subnormal. On the day after the first operation and, later, at the time when convulsions occurred the tempera ture was slightly elevated.

WEIGHT The infant was said to have weighed 6 lb, 11 oz (3,024 gm) at birth. On admission he weighed 2,710.5 gm. Since his general condition was fair, it seems strange that he should have lost such an appreciable amount of weight in so short a time, and the accuracy of the initial weighing may be doubted. He was not weighed again until the day of the second operation (four days after the first operation), when a gain of over 100 gm was recorded. Within two days of the second operation the weight had dropped almost to the 2,500 gm mark, where it remained with slight fluctuation during the rest of the investigation period.

EOSINOPHIL COUNT Unfortunately, no eosin ophil counts were performed during the first three days The count was 252/mm^3 on the fourth day and 211 mm^3 on the fifth day By the seventh post-operative day (two days after the second operation) the count dropped to 100/mm^3 and, except for a slight rise on the following day, did not rise above 100/mm^3 during the rest of the examination period. In studying adult patients Moore (1950) reported that the eosinophils usually decreased after a second operation, provided it took place within ten days of the first oper ation. Hence it was not surprising to find a low count for our patient while he was still under stress from the second operation. The noteworthy point in the record was that the count remained low during the last four days, when the child was showing clinical signs of recovery

FLUID BALANCE. In view of the fact that the child had vomited copiously prior to admission, the fluid intake was inadequate during the first four days From then onwards, the intake was adequate Although small oral feeds were occasionally given, intravenous infusions were used almost exclusively for six days On the seventh post-operative day (two days after the second operation) oral feeds were tried – the stomach being sucked out before feeds. However as most of the fluid was recovered by aspiration, we returned to intravenous infusion on the eighth day Milk feeds at half strength were started on the ninth day During the period of investigation three blood transfusions and five plasma infusions were administered. On the eighth day we gave some N/2 saline instead of the usual N/5, and on the fourteenth and fifteenth days M/6 ammonium chloride solution was infused.

Urinary output was low throughout the period of observation, and at times (on the

in the gastric aspirations. From the ninth day onwards, when adequate amounts of potassium were given in the milk, the balance was positive except on the eighth day Potassium retention was, however, never very marked and did not exceed the values for normal infants of the same age. During this period some potassium was still lost in the aspirations.

THE K N RATIO During the first eight days, when the balances were negative, the K N ratio was 8 7 meq/gm – i.e., considerably in excess of the K N ratio of lean muscle tissue. Le Quesne (1954a) stated that the K N ratio should be calculated from the relative concentrations of potassium and nitrogen in the urine. When calculating the urinary K N ratio during the first eight days, we arrived at a value of 4.5 meq/gm. It seems to us, however, that when significant losses are occurring by routes other than the renal – in this case the gastro-intestinal tract – they should be taken into account.

From the eleventh day onwards the nitrogen and potassium balances were both positive. The over-all positive balance showed a K N ratio of 3.7 meq/gm. Rather surprisingly this ratio was only slightly above the ratio for lean muscle tissue. It is possible that complete potassium restitution had not occurred by the time our studies were terminated.

Blood Studies (Table 9)

PLASMA ALKALI RESERVE AND CHLORIDE LEVEL. The excessive chloride loss in the gastric aspirations produced a steadily increasing alkalosis. Even after milk feeds had commenced and chloride retention had become marked, the alkalosis remained and the plasma chloride level continued to drop At the time we were at a loss to explain this condition. We think now that the explanation may lie in the existence of a "third fluid space" described by Randall (1952) and Kreiger *et al.* (1954) As mentioned before, these workers found that, in adults suffering from ileus, large quantities of fluid and electrolytes accumulated in the gut and were temporarily lost to the body Progressive alkalosis in our patient could therefore be explained if the milk feeds remained either partially or wholly pooled in the coils of the intestine.

On the fourteenth and fifteenth days, when the alkalosis was at its height and the child was suffering from tetany, we tried to remedy the condition by infusing M/6 ammonium chloride – Doxiadis, Goldfinch, and Holt (1953) having used this method in treating infants suffering from alkalosis due to vomiting in pyloric stenosis.

Assuming that two-thirds of the body weight was water, Forbes and Erganian (1946) had calculated that 1 ml of M/6 ammonium chloride per kg of body weight should lower the plasma alkali reserve by 0.25 meq/L. On the basis of Gamble's assumption (1951) that the extra-cellular fluid volume is equivalent to 25 per cent of the body weight, Doxiadis *et al.* (1953) calculated that 1 ml of M/6 ammonium chloride per kg of body weight should be equivalent to 0 67 meq/L of alkali reserve. It would seem, however, that this value was too high in view of the demonstration by Deane *et al.* (1952) that one-third of the total body chloride is intra-cellular If the calculation is corrected for this factor 1 ml of M/6 ammonium chloride per kg of body weight should be equivalent to 0 45 meq/L of alkali reserve. Actually, Doxiadis and his co-workers found that for every ml of M/6 ammonium chloride per kg of body weight which they infused, the alkali reserve fell by 0 43 meq/L.

Basing our procedure on their calculations, we injected 50 ml of M/6 ammonium chloride intravenously on the fourteenth day Much to our surprise, the alkali reserve fell only about 1 meq/L. On the following day we therefore injected 59 ml of M/6 ammonium chloride, but the alkali

dropped only about 2 meq/L. It is difficult to explain the difference between the response found in our patient and that found in the infants described by Doxiadis *et al.* (1953) It might be explained partly by the fact that in new born infants the extra-cellular fluid space is not 25 per cent of the body weight, as they assumed, but over 40 per cent Flexner *et al.*, 1947), and partly by our patient s inability to convert the injected ammonia quickly into urea, as we still found free ammonia in the plasma two days after the intravenous infusion. The final fall in the alkali reserve on the eighteenth and nineteenth days may have been partly due to the delayed action of the injected ammonium chloride, but were more likely due to absorption of chlorides from the intestine.

PLASMA SODIUM AND POTASSIUM LEVELS The plasma sodium concentration was low at the beginning of the study rose on the third post-operative day and then fell gradually, parallel to the chloride concentration curve, until it dropped to 115 meq/L between the tenth and the thirteenth day It then rose quickly to the normal value on the nineteenth day

The plasma potassium concentration remained nearly normal until the fourth post operative day With the onset of the intestinal obstruction which necessitated the second operation, it rapidly dropped to the hypokalaemic level of just over 2 meq/L on the fifth day After milk was given, the level rose steadily· it was above normal on the last day of the investigation.

OTHER BLOOD INVESTIGATIONS. The blood urea and plasma protein levels were above normal on the third and fourth days, owing to dehydration. On the fifth day they fell to normal. The blood urea and plasma proteins then remained at normal levels whilst the haematocrit and haemoglobin gradually fell.

CELL ELECTROLYTE LEVELS. The red cell chloride concentration remained below normal until the last two days, when it rose above the normal level. The cell sodium concentration was above normal throughout the whole period and rose to very high levels on the seventh and eighth days. The cell potassium concentration was normal at the start. It was very low between the sixth and eighth days and then rose gradually towards the normal level at the end of the period of observation.

The inverse relationship of cell sodium and cell potassium was again clearly shown.

Summary and Discussion

In this study we were able to observe a very young infant s metabolic response to repeated surgical trauma. The child not only vomited copious amounts prior to admission, but his fluid and electrolyte stores were further depleted by gastric aspiration over a long period. In order to determine whether such a gross depletion of electrolytes, and especially of potassium, would bring about a potassium shift, no solutions containing potassium were given intravenously, with the exception of the small blood and plasma transfusions containing a little potassium. Under this prolonged maximal stress, which was much in excess of anything a newborn infant had ever been subjected to in our practice, there developed a gross alkalosis culminating in tetany and a degree of hypokalaemia The data in this case are very similar to those found by Fourman (1954) in a case of potassium depletion tetany

During the first eight days the intake of nitrogen and potassium was very small or zero The output was considerable and the K N ratio greatly in excess of that of lean muscle tissue. A considerable part of the nitrogen and an even greater part of the potassium were lost in the stomach aspirations. With increasing intake, retention of both nitrogen and potassium increased, but the nitrogen retention was more marked than

CHAPTER IV

General Discussion

Before analysing the results obtained in the balance studies described in the previous chapter, two major problems must be considered. These are, first, the metabolic response to surgery found in adult patients, and second, the normal metabolism of newborn infants. Both these problems have been extensively studied during the last decade, and it is impossible to give more than a brief description of the more important work which has been done.

In the light of this review, we shall discuss some of the metabolic changes that we have observed in neonates and suggest possible underlying causes for them.

SURGICAL CONVALESCENCE OF OLDER AGE GROUPS

When discussing individual cases in the previous chapter, mention was made of some of the work on metabolism in older age groups. In addition, the earlier studies on the subject were mentioned in the introduction. It now remains to summarize some of the more recent published work.

Moore (1953a) has divided the body changes in surgical convalescence into four phases.

Phase I

In Phase I which lasts approximately three days and which Moore calls the adrenergic-corticoid phase, the following changes were noted

CLINICAL OBSERVATION Listlessness and loss of appetite, slightly elevated temperature, vasoconstriction, and ileus are characteristic. In certain types of patients — i e., those suffering from cancer of the stomach — post-operative lethargy, anorexia, and ileus are especially noticeable (Ariel *et al.*, 1943) Such patients suffer from pronounced hypochloraemia and hypoproteinaemia and are much improved by giving large amounts of protein pre-operatively In this connection, it must be remembered that it has been known for some time that the retention of fluids and crystalloids in the circulation depends to a large extent, upon the concentration of the proteins (*Lepore, 1931, Jones and Eaton, 1933*)

WEIGHT The weight drops after operation more rapidly than can be accounted for by the loss of nitrogen and water, suggesting that fat is metabolized. Whilst this observation holds good if the first three or four days are taken together, there is no doubt that during the first twenty four hours following operation the weight tends to increase quite

but Miller and Darrow (1940), Darrow (1945), and Elkinton *et al.* (1948) showed that potassium can leave the cell in signifi cant amounts if it can be excreted and that large amounts of sodium can enter the cell and replace the potassium even if there is no intake of sodium.

Further proof that increased potassium excretion is not entirely derived from destroyed tissues was brought forward by Blixenkrone-Møller (1949), who showed that, whilst potassium excretion increases mark edly six hours after operation, maximum potassium and nitrogen excretions do not coincide. These findings make it very likely that the excess potassium is, in fact, derived from the intra-cellular fluid (Wilkinson *et al.*, 1950)

Further studies of the excessive amount of potassium lost by adults and children follow ing surgery were made by Evans (1950) and Lowe *et al.* (1950) Elman *et al.* (1952) pointed out that, although most of the potassium loss occurs in the urine, some is lost in the gastro-intestinal secretions. In adults definite symptoms occur only when there is a deficiency of 200 meq or more.

Moore (1953a) found that the potassium concentration was usually normal during Phase I of the post-operative period, but Stewart and Rourke (1938) found that it decreased. That the sodium and potassium concentrations accurately reflect the concen tration of the base in the extra-cellular fluid was shown by Hastings *et al.* (1927)

It is known that some of the cell potassium is bound to protein in characteristic ratio to the cell nitrogen (Hastings and Eichelberger, 1939), but it is not known how the cell acquires a higher concentration of potassium than the extra-cellular fluid (Danowski, 1949) Potassium is, however, not the only intra-cellular base, but represents only 66 per cent, the remainder being mainly made up of magnesium (Black, 1953)

The cause of potassium loss from the cell following trauma is thought to be mainly hormonal in origin, as will be discussed later on, but Winfield *et al.* (1951), performing muscle biopsies at the start and end of opera tions, found that the muscles in the neighbourhood of the operation field lost up to 50 per cent of their potassium, whilst the muscles in distant sites lost only 10 per cent. They suggest that the high concentration of potassium in the urine may be due to the liberation of potassium from traumatized muscles.

Once potassium leaves the cell, sodium enters to replace it (Elkinton *et al.*, 1948) but this replacement compensates for only two-thirds of the lost potassium. The remain ing third of the potassium is said to be replaced by hydrogen ions (Cooke and Crow ley, 1952) In potassium depletion we may therefore meet the paradox of intra-cellular acidosis in the presence of extra-cellular alka losis (Black, 1953)

Darrow *et al.* (1948) found that in rats the serum bicarbonate concentration varied di rectly with the intra-cellular sodium and in directly with the intra-cellular potassium. Hypochloraemic alkalosis is thus a powerful stimulus for the shift of potassium — in effect producing a hypokalaemic alkalosis (Randall *et al.*, 1949 Ariel, 1954)

When potassium has passed into the extracellular space it is rapidly excreted by the kidney (Tarail and Elkinton, 1949) The excess is not only discharged by the glomeruli but also by the tubules (Mudge *et al.*, 1948) It is, however, not true that the kidney cannot conserve potassium. It can, in fact, excrete urine of lower potassium concentration than that found in plasma (Fourman, 1952)

The suggestion that a potassium shift could be caused by increased excretion of potassium by the kidney was discounted by Darrow *et al.* (1948), but Burnett, *et al.* (1950) brought forward some evidence that increased urinary excretion has an important

detail by Le Quesne (1954a) He found that on the first post-operative day sodium retention was accompanied by water retention, and that the sodium concentration of the urine was therefore paradoxically high. Late sodium retention is characterized by unaltered plasma chloride concentration, lowered urinary sodium concentration and, as a result of the sodium retention, secondary water retention. This lasts from four to six days, depending upon the severity of the operation. The chloride retention is similar to the sodium retention, but occasionally the chloride retention is in excess of the sodium retention. Potassium deficiency *per se* can cause sodium retention, as shown by Black and Milne (1952)

Coller *et al.* (1936) and Coller and Maddock (1940) have shown that the kidneys can conserve sodium chloride to a remarkable degree and under certain conditions may excrete as little as 0 1 gm per day, except on the day of operation, when the urinary chloride concentration is usually high (Le Quesne, 1954b)

The post-operative sodium and chloride balances are further complicated in patients who vomit before or after operation or who are on gastric or intestinal suction. McCann (1918) found that pyloric obstruction produced an alkalosis due to the fact that more chloride than sodium was lost in the gastric secretions. According to Moore (1949), in high intestinal obstruction the loss of sodium far outweighs the loss of potassium. Randall *et al.* (1950) have pointed out that sodium and chloride can be rapidly lost in peritonitis, and Cave (1946) has stressed the outpouring of sodium, chloride, and potassium from ileostomies. Marked sodium and potassium deficiencies therefore often develop after gastro-intestinal operations needing prolonged suction, whilst they seldom occur after thoracic surgical procedures (Aronstam *et al.*, 1953)

The hormonal control of post-operative sodium retention will be discussed below Here, it suffices to state that the retention appears, in part at least, to be due to the inflammatory reactions to injury (Wilkinson *et al.*, 1950) There is some evidence that sodium and chloride are concentrated in the damaged tissues and mobilize in the undamaged tissues of the same person (Fox and Baer, 1947)

BLOOD UREA CONCENTRATIONS The blood urea concentration rises after operation. This might be due to increased catabolism, but it is more likely due to a temporarily impaired function of the kidney (McCance and Widdowson, 1938) This view is supported by the fact that in dogs reduction of the blood supply to the kidney produces a transient renal impairment and rise in the blood urea (Van Slyke and Hiller 1947)

SERUM BILIRUBIN CONCENTRATION The serum bilirubin concentration rises after operation. This is partly due to transient impairment of liver function lasting for about a week (Tagnon *et al.*, 1948), but it may also be due to blood transfusions, as 2 per cent of the red blood corpuscles are destroyed within the first three hours (Strumia *et al.*, 1947)

CHANGES IN ICF AND IN THE ECF VOLUME. During and immediately following operation the plasma volume decreases in size, although the haemoglobin may show little change (Nelson *et al.*, 1950) This fact is of great importance when operating upon patients with chronic disease, many of whom have a reduced blood volume in spite of normal haemoglobin and haematocrit readings (Beling *et al.*, 1948) This drop in the plasma volume is followed by drops in the haematocrit and plasma protein concentrations (Ariel, 1954) Wilkinson *et al.* (1951) found that the plasma proteins fell as the plasma albumin fell and the plasma globulin concentration rose. They suggested that the drop in the plasma volume is due to transudation of

Phase II

Phase II, called the corticoid withdrawal phase by Moore (1953a), starts roughly on the fourth day after operation and usually lasts from two to three days

1. Clinically, this phase is characterized by the patient's becoming more lively and peristalsis commencing. The patient does, however, easily tire. The wound now heals and has to be cut if one wants to re-open it. In this connection it should be remembered that the tissue fluids adjacent to the wound usually have a high potassium concentration (Menkin, 1936) Even if the concentration is low, there is no delay in wound healing, as fibroblasts can grow in very varied concentrations of potassium (Findlay and Howes 1950)
2. The weight drops further, but there is now a close relation to the water and nitrogen balances.
3. The nitrogen losses are less acute, but as only small amounts of nitrogen are usually given, the balance remains negative.
4. Potassium excretion is less marked than in Phase I, and even after a small intake the balance *becomes positive, always provided* that there is no further vomiting or gastric aspiration.
5. Sodium and chloride intake is increased, and there is a marked excretion of these electrolytes. The serum sodium returns to normal in spite of increased excretion.
6. The plasma and extra-cellular fluid volumes return to normal, as has been described before, but the total body water is very slightly decreased.
7. The eosinophil count rises above the original level and then drops back to normal.

The end of Phase II is reached when retention of potassium ceases, the urinary concentration of sodium increases, and the eosinophil count returns to normal. If normal diet is now started, Phase III commences.

Phase III

Phase III, called by Moore (1953a) the spontaneous anabolic phase, is characterized as follows

1. Clinically, the patient is still weak. However, he eats well and feels strong despite his actual weakness. The caloric intake is high.
2. The potassium balance is weakly positive. It has been shown, both in animals (Cannon *et al.*, 1952) and in humans (Beal *et al.*, 1953) that protein restoration cannot occur without adequate provision of potassium for the synthesis of tissue.
3. The nitrogen balance remains steadily positive at the rate of 3 to 5 gm per day for a 70 kg man. The weight gain is correlated with the positive nitrogen balance.
4. The K N ratio is normal – 2.7 meq of potassium per gm of nitrogen.
5. The sodium and chloride balances are approximately zero
6. *The total body water increases as the lean* tissue increases.
7. The eosinophil count is normal.

Phase IV

Phase IV differs from Phase III in that fat gain has begun. The weight gain continues, with zero nitrogen and electrolyte balances the eosinophil count remains normal, and the total body water volume remains constant.

THE METABOLISM OF NEWBORN INFANTS

The newborn infant's metabolism differs in many respects from that of adults and older children. Some of the factors involved will now be discussed:

osmolarity of urine increased as more sodium, potassium, chloride, and nitrogen were excreted, the serum concentration of these substances rose. The highest blood urea reading in their series was, however, only 38 mg per cent. They deduced that premature infants are not protected from the effects of dehydration by reason of their large volume of total body water. They also noticed as an incidental finding that in infants of less than thirty-six weeks maturity the total excretion of electrolytes was two or three times that of full-term infants.

The minimal water requirements of newborn infants depend upon the renal concentrating power. An infant with an intake of 800 calories and a urinary specific gravity of 1,005 needs 171 ml per kg of body weight. With a urinary specific gravity of 1,025, however, the minimal water requirements are 94 ml per kg of body weight (Dill *et al.*, 1938)

The composition of the gastric juice in normal neonates is of considerable interest to this study, as most of our babies vomited or were on gastric suction for some time during the post-operative period. Szydlowski (1892a, b) was the first to investigate the gastric acidity of unfed newborn infants and Tangl (1906) the first to determine the pH. Miller (1941) found that the gastric acidity was high during the first days of life – 17.2 ml of N/10 HCl per 100 ml of gastric juice. It rose to a maximum of 21.6 ml N/10 HCl during the first forty-eight hours, equalling the gastric acidity of the healthy adult. It then dropped sharply and on the fifth day of life was only 0.7 ml N/10 HCl per 100 ml of gastric juice. Miller (1941) postulated that this high acidity might be due to the influence of a maternal gastrogenic hormone which reached the foetus through the placenta and which rapidly decreased in effectiveness after birth. He also stated that the birth weights of infants are closely related to the amounts of acid secreted, a statement which has been challenged by Thomson (1951), who found no relation between the pH of the gastric juice and the birth weight. This investigator determined the volume of gastric juice by aspirating the stomach shortly after birth. It ranged from 0.4 to 12.25 ml and averaged 2.65 ml.

The eosinophil count varies greatly in newborn infants but is always very much lower than in adults, it rises quickly during the first few weeks of life. The smaller and more premature the baby, the lower as a rule is the eosinophil count (Burrell, 1952, 1953). Full-term neonates show a less marked drop in the eosinophil count after the injection of ACTH than do adults, and premature babies, even less than full-term infants. Wolman (1952), performing the Thorn test on twenty four full-term infants on the day of birth, found that eight did not respond. Six of these eight, weighing under 6½ pounds, responded on the second day of life. Similar findings were reported by Bergstrand *et al.* (1952). Klein and Hanson (1950) suggested that the feeble response to ACTH indicated a diminished activity of the suprarenal gland in neonates. The response improved remarkably after the first or second week of life.

Kidney function in the newborn has been much debated, and it is possible here to mention only a few of the major contributions to this subject.

The newborn kidney is histologically immature (Gruenwald and Popper, 1940). Clara (1936) showed that the visceral layer of Bowman's capsule is cuboidal at birth and that the size and number of the capillary loops in the glomeruli are small. The number of nephrons does not increase after birth, the main post natal development of the kidney consists of an increase in the tubular tissue. The loop of Henle is short in infancy and increases in length with age (Peter, 1927).

One of the difficulties confronting investigators is the problem of how to compare the

fluenced by non renal factors and that valid comparisons with adult values are therefore not yet possible. Premature infants excrete potassium through the glomeruli and tubules (Tudvad *et al.*, 1954) As the kidneys often lose as much as 60 per cent of the amount of potassium intake (Elman *et al.*, 1952), there is no greater danger in giving potassium to premature infants than in giving it to full term ones.

The kidney function of neonates should not be judged by the blood urea. Increased nitrogen intake (Barnett and Vesterdal, 1953), tissue breakdown (McCance and Widdowson, 1947), reduction in urea clearance due to dehydration (Black *et al* 1944), and variation in the rate of urine flow (Barnett and Vesterdal, 1953) can all cause a rise in blood urea. Starvation probably explains in part the low nitrogen excretion of newborn infants, but the need for nitrogen to build up tissues is chiefly responsible (Barlow and McCance, 1948)

Whilst the above description appears to show that the newborn infant's kidney is rather immature, it must be remembered that in all the above investigations the basis of comparison was surface area. On the basis of total body water, McCance *et al.* (1954) found that the human infant's kidney is more mature than those of animals. They also noted that, when given large doses of water, infants excrete urine as rapidly as adults the urine is equally dilute, and the glomerular infiltration rate the same. Infants differ from adults in that the volume of urine excreted by them within a period of four to five and one-half hours falls short of the test dose. In other words, although the neonatal kidney is immature, it is not so under-developed as was formerly thought.

There might be some criticism about including a Mongol in the present series in view of the opinion expressed by Benda (1946) and Roosen-Runge (1949) that the kidneys of children with congenital cerebral defects are small when compared with those of normal children and that there is retardation of glomerular and tubular differentiation. Both these authors, however, point out that these differences are most apparent in older children (five years of age and over one year, respectively) On the other hand, Vesterdal and Tudvad (1949) studied the glomerular filtration rate in infants under three months of age and found that two Mongols had clearances comparable with those of normal infants. Calcagno and Rubin (1951), on studying the effect of dehydration upon the renal function in seven infants, of whom four were Mongols and two mental defectives, found that the normal baby in the series behaved like the others. We therefore felt justified in including the Mongol baby in our investigation.

RESULTS OBTAINED IN THE PRESENT INVESTIGATION

In discussing our results and comparing the metabolic response to surgery in newborn infants with that reported for adults, stress will be laid on those points where the two responses are dissimilar

Our investigations were of necessity short and usually covered only Phase I and part of Phase II of Moore's (1953a) classification of convalescence. As the most important changes occur during these phases, this curtailment of our studies is perhaps not too serious.

From the clinical point of view newborn infants stand prolonged operations extraordinarily well and usually are very lively a few hours after operation. It is difficult to say anything definite about their appetite, but there is no doubt that they are very likely to vomit for several days following operation This tendency and the subsequent danger of aspirating the vomitus are undoubtedly the

purpose of maintaining a normal plasma volume and restoring the plasma protein concentration.

It must be remembered that in starvation, such as occurred post-operatively in most of our cases, the plasma volume decreases before the plasma protein concentration falls (Madden *et al.*, 1940) When the plasma proteins fall, plasma infusion will restore the concentration to normal (Allen *et al.*, 1948)

Once there is an adequate nitrogen intake by mouth, nitrogen retention occurs. The normal newborn infant retains nitrogen to a marked extent and behaves in this respect like an adult in Phase II (Moore, 1953a) of the post-operative state.

The blood urea, both before and after operation, tends to rise to comparatively high levels, although there is little or no dehydration, and one has to assume that increased protein breakdown and variation in the renal function play a part.

In adults the "potassium shift" described above represents the characteristic change in the K.N ratio during the post-operative period. As a result, more potassium leaves the cell than is liberated by tissue breakdown and excreted by the kidney, which cannot retain it to any marked degree. The post operative K.N ratio is therefore considerably in excess of the value for normal lean muscle tissue. In this respect our most significant finding was that none of the six infants who were operated upon shortly after birth lost an excessive amount of potassium, despite the fact that the majority had required extensive surgery and were seriously ill post-operatively Indeed three were so ill that they failed to recover Nevertheless, in the post-operative negative phase all six infants showed a K N ratio within the range for lean muscle tissue. It might be objected that potassium and nitrogen present in the meconium, which are not derived from post natal tissue breakdown, were included in the total balance during the first few days of life. But calculation of the K N ratio during the negative phase, excluding the meconium, gives lower values than those obtained from the total balance. It appears, therefore, that in general these newborn infants lost nitrogen and potassium because they were starving and that no other mechanism came into play

An entirely different response to surgical trauma was shown by Cases 2 and 3, who were operated upon when they were more than three weeks old and whose reactions followed the adult pattern It would therefore seem that ability to maintain a normal K N ratio after surgery does not last for very long after birth. That this is not invariably true is shown by the data on Case 8 Although this infant was over three weeks old at the time of operation, the K N ratio followed the neonatal pattern described above. This pattern is somewhat similar to that of depleted adult patients who have been ill for a long time before surgery and who also tend to maintain a K N ratio which approximates the values of lean muscle tissue (Moore and Ball, 1952) However the immediate post-operative progress of the neonate, unlike that of the depleted adult patient, is usually very good.

There are four possible explanations for this phenomenon in newborn infants The infant's muscle may be depleted of potassium at birth, the potassium may be bound more firmly to the foetal protein, the foetal kidney may be incapable of excreting the potassium lost from the muscles, or the hormonal control and hence the metabolic changes in neonates may differ from those of adults and older children

The first possibility can be discounted. McCance *et al.* (1954) have shown that newborn infants muscles contain potassium slightly in excess of that found in adults. We found that the red blood corpuscles of newborn babies had potassium concentrations a

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under 3 meq/L certainly indicate potassium depletion, but a high, normal, or slightly subnormal level might be encountered in a negative as well as a positive balance phase

As in adults, post-operative retention of sodium and chloride is common. There are, however, some points worth noting in relation to newborn infants Sodium and chloride retention does not occur on the day of operation. Storage of sodium and chloride usually starts one or two days after operation As has been mentioned previously, some neonates are very prone to acidosis and tend to retain considerably more chloride than sodium. The *ensuing acidosis does not appear* to have any serious clinical effects Retention of sodium is thought to be accompanied by expansion of the extra-cellular space, and certainly the weight changes in some of our patients following operation point towards considerable water retention Gastric and intestinal aspirations of neonates contain a considerable quantity of sodium and even more chloride. Continuous gastric suction will therefore deplete the body of these ions, and hypochloraemic alkalosis will result. However, in order to produce a serious degree of alkalosis, gastric suction must continue for many days.

In the *older neonates* (*i.e.*, those over three weeks – Cases 2, 3, and 8) the eosinophil response to trauma resembled that found in adults – i.e., an immediate post-operative drop to very low levels, followed by a gradual rise, often to levels above the initial one. In infants who were only a few days old the eosinophil response was most irregular and appeared not to have any connection with the severity of the condition or with clinical improvement or deterioration. These observations supported the finding of Jailer *et al.* (1951) that the eosinophil response of new born infants to ACTH showed wide variations. It therefore seemed obvious that the eosinophil count would be of *no practical* value for testing neonatal reactions during the post-operative period.

THE ENDOCRINE RESPONSE TO INJURY

It remains for us to discuss briefly the possible hormonal control of the metabolic response to surgery in newborn infants In order to elucidate this problem we have to mention some of the work which has been done on adults and neonates.

It was Cannon (1915 1932) who first directed attention to the neuro-endocrine response to injury and stress and Selye (1936, 1946) who by introducing his concept of the "alarm reaction," did so much to stimulate research into these problems.

Activity of the posterior pituitary antidiuretic hormone was first demonstrated by Verney (1946a, b, 1947), and Burnett *et al.* (1949) showed that the hormone is released as the result of anaesthesia. Operative trauma has the same effect (Ariel and Miller, 1950), so has pain (Kelsall, 1949, Chalmers and Lewis, 1951), and so have morphia and pethidine injections (Habif *et al.*, 1951)

The anti-diuretic hormone has no effect upon sodium retention and potassium excretion (Chalmers *et al.*, 1951, Hayes and Coller, 1952)

There is considerable evidence that post operative sodium retention and potassium excretion in adults are adreno-cortical in origin (Johnson *et al.* 1950) The eosinophil count falls and urinary excretion of corticoids and keto-steroids increases after operation (Hardy *et al.*, 1953) Administration of these hormones should therefore increase the extracellular fluid space and decrease the total body water This was shown to be so in animal experiments by Gaudino and Levitt (1949)

The secretion of adreno-cortical hormones *appears to be controlled by secretion of*

stress shows that his resistance is high. Whatever the cause of this resistance, be it due to physiological processes in the foetus or to the action of hormones secreted by the mother and conveyed to the foetus through the placenta, it wears off some days after birth. During this neonatal period, however the infant shows striking differences in his hormonal equilibrium and metabolism. He is endowed with marked resistance to trauma and stress, which is reflected in his metabolic response to surgery

single trauma with gratifying convalescence, provided the surgeon does nothing to interrupt the compensatory mechanism of nature" He stressed the need to leave the patient alone.

The dangers of over treatment are particularly marked in neonatal surgery By far the most common cause of death following this type of surgery is pneumonia, and this is not infrequently due to over-enthusiastic administration of intravenous infusions (Louw *et al.*, 1954)

On the other hand, unqualified rejection of intravenous therapy in surgical practice would be a retrograde step In our opinion, when complications occur it is not the therapy but the therapist who is at fault. We therefore believe that it devolves upon the surgeon to take a greater interest in the subject. As Lockwood and Randall (1949) have so aptly stated "The surgeon who is ambitious to maintain his mortality at an irreducible *minimum must be just as* much concerned with the necessity for physiological fluid replacement therapy as with technical details of the surgical procedure itself"

Temperature

Newborn infants in general and premature infants in particular have comparatively undeveloped temperature-regulating centres (Smith, 1951) Their body temperatures are often inconsistent and tend to fluctuate with the environmental temperature. Moreover because of the neonate's relatively large body surface, high metabolic rate, and small amount of subcutaneous fat, heat loss from the body is more rapid than in adults and older children.

These facts have been realized for a long time and it has therefore been standard practice to protect infants from heat loss during and following operation by clothing them in thick layers of Gamgee tissue or cotton wool, surrounding them with hot water bottles, or nursing them on electric blankets. However, there are several theoretical objections to these procedures. First, when a person is shocked by operative trauma, circulation to the vital centres is dependent upon a reduced blood supply, and dilatation of the subcutaneous vessels by application of heat therefore does not improve his condition. The contrary is the case. Second, a fall in body temperature reduces the basal metabolism and decreases the oxygen consumption on theoretical grounds it is therefore beneficial (quite apart from its application to cardiac surgery) in prolonged operations on seriously ill patients. Third, as Miller *et al.* (1954) have shown, hypothermia increases neonatal resistance to anoxia. For some years it has been our practice not to protect our infants from heat loss during operation. Whilst we do not actively cool them, the absence of protection from heat loss results in a conspicuous lowering of body temperature, especially in small infants. *This* has facilitated anaesthesia and post-operative recovery and has certainly not increased the incidence of post-operative pneumonia.

After operation the babies are placed in incubators in which they can be tended, nursed, and x rayed without change of environment (Fig. 3 see insert, Chapter II) This has several advantages

1 A constant temperature (usually 85° F) can be maintained. This allows the infant to be nursed naked. As we use no dressings except ½ inch plastic tape, constant inspection of the abdomen and of the rate and type of respiration can be maintained. Moreover, unrestricted by clothing, the infant can move freely
2. Draughts are avoided.
3 A definite concentration of oxygen can be maintained if necessary
4. Most important of all, an atmosphere of 100 per cent humidity can be maintained.

come this difficulty Todd (1953) tried infusions of 10 per cent invert sugar, which are rapidly metabolized and less likely to cause thrombosis of the veins. This sugar has certainly proved to be of value in infants suffering from gastro-enteritis, who are very much dehydrated and need large quantities of fluids. We, too, have used 10 per cent invert sugar solutions for neonates during the post-operative period. Although we found it to be an improvement on 10 per cent glucose, thromboses sometimes occurred when the infusion was given at the very slow rate required by our technique. Furthermore, even a 10 per cent invert sugar solution will not provide sufficient calories when the total daily fluid intake is small. We have not yet used emulsified fat infusions, as they are still in the experimental stage in this country A really satisfactory preparation would be of great benefit to neonatal surgery

In our experience it has therefore been impossible to provide newborn infants with an adequate caloric intake by intravenous infusion. This fact alone made it imperative to commence oral feeding as soon as possible. The immediate changes in caloric intake, once milk feeds were used, are shown in the cases described above. Fortunately because of the tolerance of neonates to low caloric intake and also because we have seldom had to rely solely on intravenous alimentation for longer than ten days at the most, this problem has never been a very serious one. The routine use of 5 per cent glucose solutions, coupled with occasional blood and plasma transfusions, appears on the whole adequate to tide the baby over the immediate post operative period as far as the caloric intake is concerned.

Finally, we have to mention the possibility of providing calories by intravenous infusion of protein hydrolysates. This will be discussed in some detail in relation to nitrogen metabolism.

Fluid Requirements

It is in estimating the post-operative fluid requirements of newborn infants that most mistakes have been made in the past. Surgeons and paediatricians have often not realized how very small are the newborn baby's fluid requirements, how little dehydration harms him, and how easily he can be over-transfused. Many an excellently performed operation has been marred by subsequently drowning the infant with excessive intravenous therapy

The widely taught rule, that an infant's fluid requirements are 2½ ounces per pound of body weight does not apply to neonatal surgery or for that matter to the immediate post natal period of normal infants. The urinary output is very small at first and rises only gradually to what are regarded as normal levels. The fluid requirements during the first weeks of life are also very small. They are even smaller, actually and proportionately, in premature infants.

Post-operative water retention is not as marked in neonates as it is in adults but it does occur and further reduces the already very small fluid requirements. Very great care must therefore be taken in assessing and treating dehydration and replacing fluid losses

The clinical diagnosis of dehydration is usually not difficult. Dehydration produces clinically recognizable signs more rapidly in infants than in adults, although it must be remembered that when dehydration is obvious, 6 per cent of the body water has already been lost (Darrow 1940) Although the blood urea level has proved a reliable guide to the state of hydration in adults (Homann, 1951) the rise is so rapid in neonates that it may give an erroneous impression of the severity of the infant's condition. A reading of over 100 mg per cent is often encountered in an infant with minimal clinical dehydration As has been pointed out

point of measuring and charting the quantities not as drops per minute (an inaccurate method, as the size of drops is very variable) but as ml per hour It is also obvious that at this slow rate intravenous infusions are very likely to stop unless there is constant, careful, and skilled nursing supervision and unless a two-way tap with a syringe attachment is incorporated in the infusion set.

Finally, we have to touch upon the questions whether dehydration should be corrected pre-operatively and to what extent pre-operative intravenous therapy should be given. Louw *et al.* (1954) have stated that dehydration must be corrected before operation. We find that in cases of simple water loss, as in oesophageal atresia, this is often unnecessary Infants five and six days old will often stand the operation without any pre-operative fluid replacement. Infants suffering from intestinal obstruction present a very different problem. Here the losses by vomiting must certainly be made good before operation can be contemplated, but the loss of water is much less important than the loss of electrolytes (see below)

In view of the great hazards of post-operative *infusions*, it cannot be over-emphasized that the sooner the intravenous infusion is discontinued and oral feeding started the better is the chance of recovery Unfortunately, many abdominal operations upon neonates in which the intestines are opened are followed by prolonged periods of ileus and intravenous therapy must be continued. In this connection it should be stressed that great as are the dangers of intravenous infusions for newborn infants, the dangers of vomiting and inhaling the vomitus during the post operative period are even greater Gastric aspirations (and hence intravenous infusions) should therefore never be discontinued until the surgeon is absolutely sure that the ileus (whether mechanical or paralytic) has been overcome.

The Nitrogen Requirements

The newborn infant loses weight and breaks down proteins for some time after birth and this catabolic phase cannot be reversed by a high protein intake. Operation during this period slightly increases the nitrogen excretion. When the post-operative adreno-cortical phase is short, there is no need to worry about this nitrogen loss, but if it is prolonged, the replacement of nitrogen becomes of great importance. Our experience with the infusions of protein hydrolysates was an unhappy one, since all the preparations we tried were very irritating to newborn infants veins. Reconstructed dried plasma has proved much more satisfactory Diluted with an equal amount of distilled water in order to lower the electrolyte content, the plasma is infused in quantities of 50 to 100 ml per day according to the size of the baby As pointed out in a previous chapter, plasma infusion quickly restores the plasma volume in neonates and also raises the plasma protein concentration, which rapidly falls when the babies are starved.

No intravenous infusion can do more than tide the child over until it can take milk orally In those children who cannot take milk (i.e., certain cases of meconium ileus, who are very intolerant to pancreatin by mouth) oral feeding with protein hydrolysates has occasionally been quite successful.

Under this heading we should like to mention briefly the question of blood replacement which has been previously discussed in some detail (Rickham, 1954a) At birth, infants have a very high haematocrit and haemoglobin concentration. In spite of this, blood loss during operation should be meticulously replaced. While over infusion is definitely harmful, we have seen no ill-effects from slight over transfusion during operation. The explanation may lie in the fact that post-operatively newborn infants can speedily destroy their red blood corpuscles. We be-

...ponses. Each case has to be treated on its merits after careful clinical and laboratory evaluation. It is clearly beyond the scope of many laboratories to perform balance tests such as the ones here described, but in practice it has been found that only a very few biochemical tests are necessary in order to ensure satisfactory post operative management. Although an occasional haemoglobin reading or estimation of plasma potassium may be of use, such tests are infrequently employed. Experience has taught us to rely almost entirely on four biochemical tests – namely, the blood urea, the plasma alkali reserve, and the plasma chloride and protein concentrations. If the rules laid down above are borne in mind and the patient's intake and output are accurately measured, these four tests are entirely sufficient to deal with the most complicated post-operative problems.

To illustrate this point we have added a tenth case to the present series. The post operative metabolic changes of Case 10 were adequately controlled, although only the basic tests mentioned above were routinely employed. This case was specifically chosen because the patient not only underwent two major operations, but also suffered from prolonged ileus, necessitating continuous gastric suction and intravenous therapy for ten days Furthermore, she had suffered from high intestinal obstruction and hence vomited copiously before operation. We feel that, if it is possible to control an infant's biochemistry under such difficult circumstances, using only a few standard tests, it should be feasible in practically all cases.

Before discussing this case in more detail, it should be pointed out that although the tests we routinely employ are few in number, they must be performed with accuracy and in a laboratory with facilities to handle ultra-micro tests. Furthermore, none of these tests are of any practical value unless the results can be obtained within a very few hours and unless the laboratory staff is ready to help at any time of the day or night. It is our firm conviction that unless a surgeon can rely on such laboratory facilities he is most unwise to operate upon newborn infants.

CASE 10 (VIVIAN A)

History

The infant was admitted to the Neonatal Surgical Unit at the age of eight days, with a history of having vomited bile-stained material since birth. She had passed several meconium stools

A provisional diagnosis of partial duodenal obstruction was confirmed by radiography

The operation was performed on the day of admission, at which time a perforated septum in the third part of the duodenum was excised and a duodeno-duodenostomy performed.

Post-operatively large quantities of bile-stained material were obtained by gastric aspiration, and on the sixth day it became obvious that the anastomosis was not working Consequently at a second operation a duodeno-jejunostomy was performed. After a period of paralytic ileus lasting three days, the child made an uninterrupted recovery

Discussion (See Table 10)

The blood samples for chemical analysis were taken each morning The intravenous therapy was planned on the basis of the biochemical data and the clinical findings. On admission the blood urea concentration was 47 mg per 100 ml, and mild dehydration was clinically apparent. The first operation was performed after six hours of intravenous therapy

Post-operatively the considerable amount of fluid aspirated from the stomach necessitated a larger intravenous infusion than we usually give

With the intravenous régime outlined in

Appendix

The composition of the various fluids used for oral and intravenous administration in o investigation has only been loosely referred to in the text. A more detailed description given in this Appendix.

SALINE. When the word saline is mentioned in the text either for oral or intraveno use, N/5 saline was used – i.e., a solution containing 29 1 meq/L. Specific mention made in the text to the few occasions on which N/2 saline (containing 72.7 meq/L) w used. Normal saline was not used.

DARROW S SOLUTION The Darrow s solution used during this investigation had the f lowing composition

Potassium chloride	35 7 meq/L
Sodium chloride	68.5 meq/L
Sodium lactate	53.3 meq/L

PLASMA. The plasma infusions referred to in the text consisted of dried plasma reconst tuted with double the usual amount of distilled water

BLOOD The blood used was stored blood. In this connection it should be noted that amount of plasma and blood shown in the fluid intake charts refers not to the total amou given but only to the water content.

MILK. The milk mixtures used were made up from milk powder supplied to us i batches of uniformly mixed powder bulk analysed by the laboratory of the Cow an Gate Company As our studies extended over a lengthy period, it was necessary to r place the original milk powder by a fresh supply These two batches of milk powd varied considerably in their composition.

To make up feeds we dissolved 1 gm of the powder in 10 ml of water The resultin milk mixture is referred to in the text as full-strength milk. Occasionally we used hal strength milk mixture containing only 0.5 gm of the powder per 10 ml of water

The composition of the full-strength milk mixtures was as follows

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